

# 45991 JAN SEARCH REQUEST FORM

Requestor's Name: FCNDA 71970 Serial Number: 09/712364  
 Date: 0-4-01 Phone: 28-1620 Art Unit: 1623  
Room NO Box: CM1 8B19

## Search Topic:

Please write a detailed statement of search topic. Describe specifically as possible the subject matter to be searched. Define any terms that may have a special meaning. Give examples or relevant citations, authors, keywords, etc., if known. For sequences, please attach a copy of the sequence. You may include a copy of the broadest and/or most relevant claim(s).

bib, assignee data attached.

please search attached claims 21-25.

See my notes on the claims for specifications -  
 not much provided. Note that claim 25

is broad enough to encompass co-administration  
 of any two compounds that reduce serum  
 cholesterol.

Thanks

Dear Examiner,  
 You can help us in our efforts to get searches back to you in a timely manner by including your art unit  
 and room number on all searches you submit to the STIC.  
 Thanks from the STIC-Biotech/Chemistry Library

## STAFF USE ONLY

Date completed: 6/23/01  
 Searcher: W  
 Terminal time: \_\_\_\_\_  
 Elapsed time: \_\_\_\_\_  
 CPU time: 3.0  
 Total time: 4.5  
 Number of Searches: \_\_\_\_\_  
 Number of Databases: \_\_\_\_\_

Search Site  
 \_\_\_\_\_ STIC  
☒ CM-1  
 \_\_\_\_\_ Pre-S  
 Type of Search  
 \_\_\_\_\_ N.A. Sequence  
 \_\_\_\_\_ A.A. Sequence  
 \_\_\_\_\_ Structure  
☒ Bibliographic

Vendors  
 \_\_\_\_\_ IG  
☒ STN  
 \_\_\_\_\_ Dialog  
 \_\_\_\_\_ APS  
 \_\_\_\_\_ Geninfo  
 \_\_\_\_\_ SDC  
 \_\_\_\_\_ DARC/Questel  
 \_\_\_\_\_ Other

=> fil reg

FILE 'REGISTRY' ENTERED AT 12:01:32 ON 23 JUN 2001  
 USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.  
 PLEASE SEE "HELP USAGETERMS" FOR DETAILS.  
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STRUCTURE FILE UPDATES: 22 JUN 2001 HIGHEST RN 343216-50-2  
 DICTIONARY FILE UPDATES: 22 JUN 2001 HIGHEST RN 343216-50-2

TSCA INFORMATION NOW CURRENT THROUGH January 11, 2001

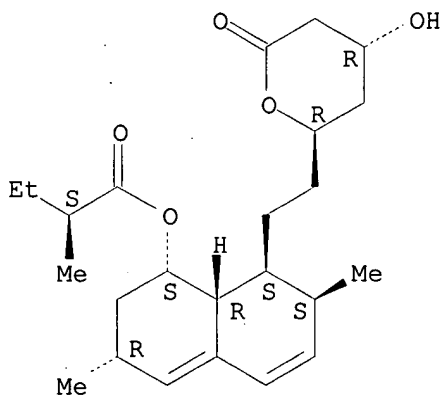
Please note that search-term pricing does apply when  
 conducting SmartSELECT searches.

Structure search limits have been increased. See HELP SLIMIT  
 for details.

=> d ide can tot

L85 ANSWER 1 OF 40 REGISTRY COPYRIGHT 2001 ACS  
 RN 316381-08-5 REGISTRY  
 CN Butanoic acid, 2-methyl-, (1S,3R,7S,8S,8aR)-1,2,3,7,8,8a-hexahydro-  
 3,7-dimethyl-8-[2-[(2R,4R)-tetrahydro-4-hydroxy-6-oxo-2H-pyran-2-yl]ethyl]-  
 1-naphthalenyl ester, labeled with tritium, (2S)- (9CI) (CA INDEX  
 NAME)  
 FS STEREOSEARCH  
 MF C24 H36 O5  
 SR CAS Registry Services  
 LC STN Files: CHEMCATS  
 IL XH-3

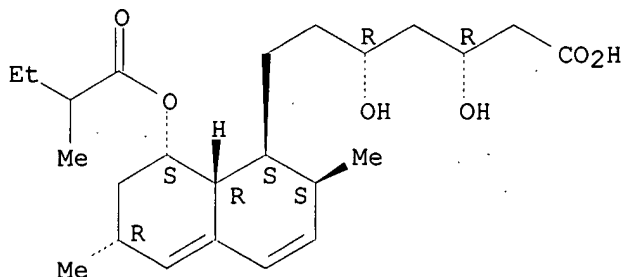
Absolute stereochemistry.



Point of Contact:  
 Jon  
 Librarian-Physical Sciences  
 CM1 1E01 Tel: 308-4498

L85 ANSWER 2 OF 40 REGISTRY COPYRIGHT 2001 ACS  
 RN 314729-27-6 REGISTRY  
 CN 1-Naphthaleneheptanoic acid, 1,2,6,7,8,8a-hexahydro-.beta.,.delta.-  
 dihydroxy-2,6-dimethyl-8-(2-methyl-1-oxobutoxy)-,  
 (.beta.R,.delta.R,1S,2S,6R,8S,8aR)- (9CI) (CA INDEX NAME)  
 FS STEREOSEARCH  
 MF C24 H38 O6  
 CI COM  
 SR CA  
 LC STN Files: CA, CAPLUS, CASREACT

Absolute stereochemistry.

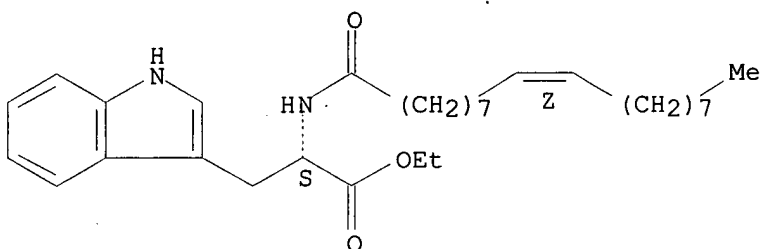


1 REFERENCES IN FILE CA (1967 TO DATE)  
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 134:71492

L85 ANSWER 3 OF 40 REGISTRY COPYRIGHT 2001 ACS  
RN **261734-93-4** REGISTRY  
CN L-Tryptophan, N-[(9Z)-1-oxo-9-octadecenyl]-, ethyl ester (9CI) (CA INDEX NAME)  
FS STEREOSEARCH  
MF C31 H48 N2 O3  
SR CA  
LC STN Files: CA, CAPLUS, TOXLIT

Absolute stereochemistry.  
Double bond geometry as shown.

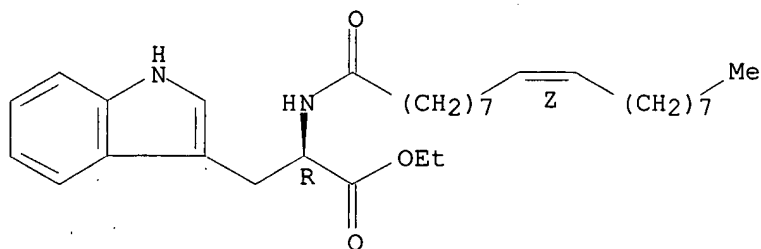


1 REFERENCES IN FILE CA (1967 TO DATE)  
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 132:231975

L85 ANSWER 4 OF 40 REGISTRY COPYRIGHT 2001 ACS  
RN **261734-92-3** REGISTRY  
CN D-Tryptophan, N-[(9Z)-1-oxo-9-octadecenyl]-, ethyl ester (9CI) (CA INDEX NAME)  
FS STEREOSEARCH  
MF C31 H48 N2 O3  
SR CA  
LC STN Files: CA, CAPLUS, TOXLIT

Absolute stereochemistry.  
Double bond geometry as shown.

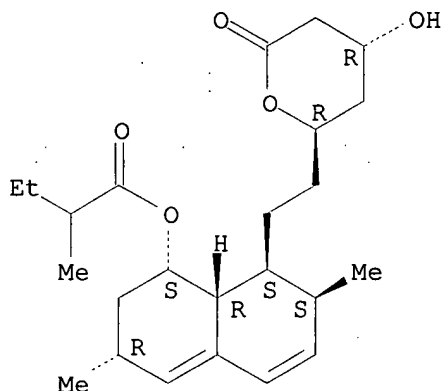


1 REFERENCES IN FILE CA (1967 TO DATE)  
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 132:231975

L85 ANSWER 5 OF 40 REGISTRY COPYRIGHT 2001 ACS  
RN 237073-61-9 REGISTRY  
CN Butanoic acid, 2-methyl-, (1S,3R,7S,8S,8aR)-1,2,3,7,8,8a-hexahydro-3,7-dimethyl-8-[2-[(2R,4R)-tetrahydro-4-hydroxy-6-oxo-2H-pyran-2-yl]ethyl]-1-naphthalenyl ester (9CI) (CA INDEX NAME)  
FS STEREOSEARCH  
MF C24 H36 O5  
SR CA  
LC STN Files: CA, CAPLUS, CASREACT, USPATFULL

Absolute stereochemistry.



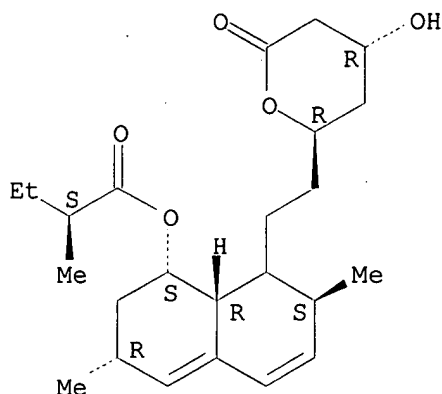
2 REFERENCES IN FILE CA (1967 TO DATE)  
2 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 134:71492

REFERENCE 2: 131:157706

L85 ANSWER 6 OF 40 REGISTRY COPYRIGHT 2001 ACS  
RN 214357-28-5 REGISTRY  
CN Butanoic acid, 2-methyl-, (1S,3R,7S,8aR)-1,2,3,7,8,8a-hexahydro-3,7-dimethyl-8-[2-[(2R,4R)-tetrahydro-4-hydroxy-6-oxo-2H-pyran-2-yl]ethyl]-1-naphthalenyl ester, (2S)- (9CI) (CA INDEX NAME)  
FS STEREOSEARCH  
MF C24 H36 O5  
SR CA  
LC STN Files: CA, CAPLUS

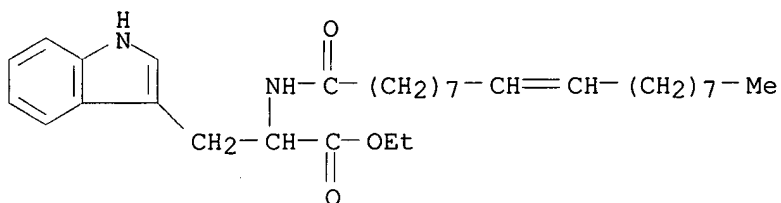
Absolute stereochemistry.



1 REFERENCES IN FILE CA (1967 TO DATE)  
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 129:290016

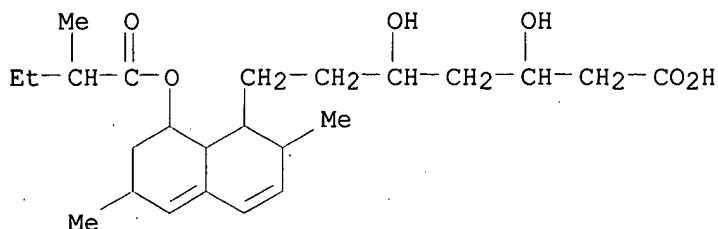
L85 ANSWER 7 OF 40 REGISTRY COPYRIGHT 2001 ACS  
RN 202401-34-1 REGISTRY  
CN Tryptophan, N-(1-oxo-9-octadecenyl)-, ethyl ester (9CI) (CA INDEX NAME)  
FS 3D CONCORD  
MF C31 H48 N2 O3  
SR CAS Registry Services  
LC STN Files: CA, CAPLUS, CHEMCATS, TOXLIT



1 REFERENCES IN FILE CA (1967 TO DATE)  
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 134:371771

L85 ANSWER 8 OF 40 REGISTRY COPYRIGHT 2001 ACS  
RN 137767-34-1 REGISTRY  
CN 1-Naphthaleneheptanoic acid, 1,2,6,7,8,8a-hexahydro-.beta.,.delta.-dihydroxy-2,6-dimethyl-8-(2-methyl-1-oxobutoxy)- (9CI) (CA INDEX NAME)  
OTHER NAMES:  
CN L 665465  
MF C24 H38 O6  
SR CA  
LC STN Files: BEILSTEIN\*, CA, CAPLUS, TOXLIT  
(\*File contains numerically searchable property data)



2 REFERENCES IN FILE CA (1967 TO DATE)  
2 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 116:51291

REFERENCE 2: 116:537

L85 ANSWER 9 OF 40 REGISTRY COPYRIGHT 2001 ACS

RN 123049-73-0 REGISTRY

CN Butanoic acid, 2-methyl-, 1,2,3,7,8,8a-hexahydro-3,7-dimethyl-8-[2-(tetrahydro-4-hydroxy-6-oxo-2H-pyran-2-yl)ethyl]-1-naphthalenyl ester, [1S-[1.alpha. (R\*), 3.beta., 7.beta., 8.beta. (2S\*, 4S\*), 8a.beta.]]- (9CI)  
(CA INDEX NAME)

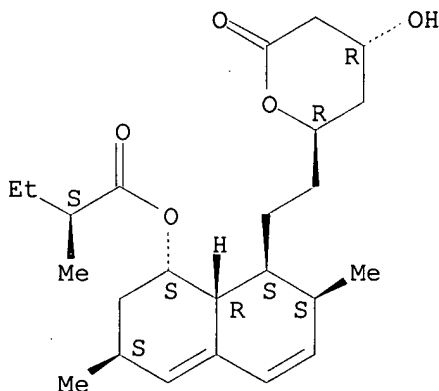
FS STEREOSEARCH

MF C24 H36 O5

SR CA

LC STN Files: BEILSTEIN\*, CA, CAPLUS, CHEMINFORMRX  
(\*File contains numerically searchable property data)

Absolute stereochemistry.



2 REFERENCES IN FILE CA (1967 TO DATE)  
2 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 121:204880

REFERENCE 2: 111:173984

L85 ANSWER 10 OF 40 REGISTRY COPYRIGHT 2001 ACS

RN 105227-51-8 REGISTRY

CN Butanoic acid, 2-methyl-, 1,2,3,7,8,8a-hexahydro-3,7-dimethyl-8-[2-(tetrahydro-4-hydroxy-6-oxo-2H-pyran-2-yl)ethyl]-1-naphthalenyl ester, [1S-[1.alpha. (R\*), 3.alpha., 7.beta., 8.beta. (2R\*, 4S\*), 8a.beta.]]- (9CI)  
(CA INDEX NAME)

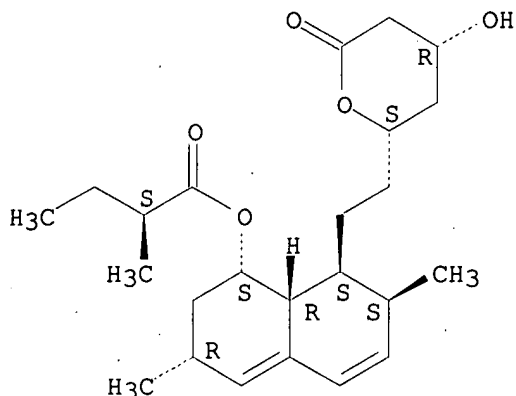
FS STEREOSEARCH

MF C24 H36 O5

SR CA

LC STN Files: BEILSTEIN\*, CA, CAPLUS, CASREACT, CHEMINFORMRX  
(\*File contains numerically searchable property data)

Absolute stereochemistry.



2 REFERENCES IN FILE CA (1967 TO DATE)  
2 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 111:133822

REFERENCE 2: 106:49852

L85 ANSWER 11 OF 40 REGISTRY COPYRIGHT 2001 ACS

RN **94921-32-1** REGISTRY

CN Tryptophan, N-(1-oxo-9-octadecenyl)-, ethyl ester, (E)- (9CI) (CA INDEX NAME)

OTHER CA INDEX NAMES:

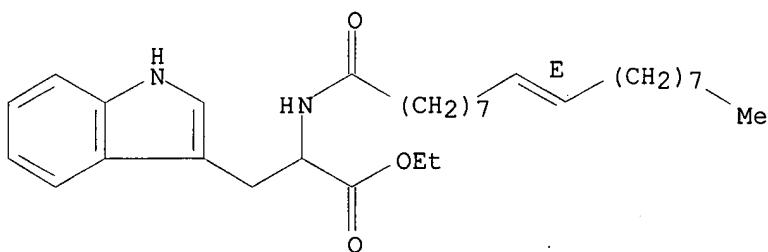
CN DL-Tryptophan, N-(1-oxo-9-octadecenyl)-, ethyl ester, (E)-

FS STEREOSEARCH

MF C31 H48 N2 O3

LC STN Files: BEILSTEIN\*, CA, CAPLUS, TOXLIT  
(\*File contains numerically searchable property data)

Double bond geometry as shown.



1 REFERENCES IN FILE CA (1967 TO DATE)  
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 102:89686

L85 ANSWER 12 OF 40 REGISTRY COPYRIGHT 2001 ACS

RN 83213-71-2 REGISTRY

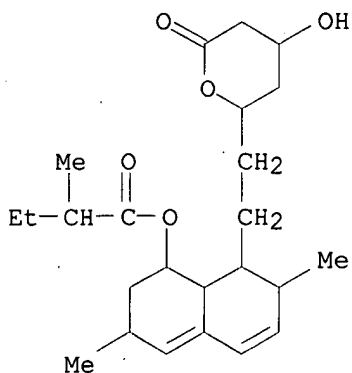
CN Butanoic acid, 2-methyl-, 1,2,3,7,8,8a-hexahydro-3,7-dimethyl-8-[2-(tetrahydro-4-hydroxy-6-oxo-2H-pyran-2-yl)ethyl]-1-naphthalenyl ester (9CI) (CA INDEX NAME)

OTHER NAMES:

CN Monarubin

MF **C24 H36 O5**

LC STN Files: BEILSTEIN\*, CA, CAPLUS, CHEMINFORMRX  
(\*File contains numerically searchable property data)



1 REFERENCES IN FILE CA (1967 TO DATE)  
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 101:130443

L85 ANSWER 13 OF 40 REGISTRY COPYRIGHT 2001 ACS

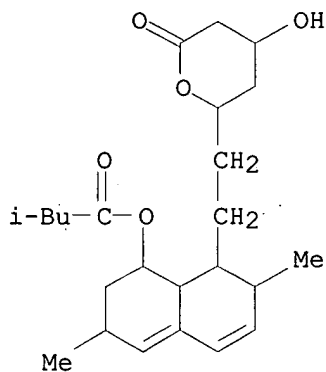
RN 81202-26-8 REGISTRY

CN Butanoic acid, 3-methyl-, 1,2,3,7,8,8a-hexahydro-3,7-dimethyl-8-[2-(tetrahydro-4-hydroxy-6-oxo-2H-pyran-2-yl)ethyl]-1-naphthalenyl ester (9CI) (CA INDEX NAME)

MF C24 H36 O5

LC STN Files: BEILSTEIN\*, CA, CAPLUS

(\*File contains numerically searchable property data)



2 REFERENCES IN FILE CA (1967 TO DATE)  
2 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 97:23627

REFERENCE 2: 96:181078

L85 ANSWER 14 OF 40 REGISTRY COPYRIGHT 2001 ACS

RN 79952-44-6 REGISTRY

CN Butanoic acid, 2-methyl-, 1,2,3,7,8,8a-hexahydro-3,7-dimethyl-8-[2-(tetrahydro-4-hydroxy-6-oxo-2H-pyran-2-yl)ethyl]-1-naphthalenyl ester, [1S-[1.alpha.(S\*),3.alpha.,7.beta.,8.beta.(2S\*,4S\*),8a.beta.]]- (9CI) (CA INDEX NAME)

FS STEREOSEARCH

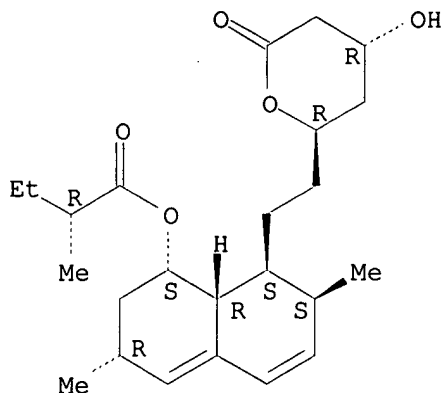
MF C24 H36 O5

LC STN Files: BEILSTEIN\*, CA, CAPLUS, CASREACT, CHEMINFORMRX, TOXLIT, USPATFULL

(\*File contains numerically searchable property data)

Absolute stereochemistry.





9 REFERENCES IN FILE CA (1967 TO DATE)

9 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 111:133822

REFERENCE 2: 110:18101

REFERENCE 3: 104:186228

REFERENCE 4: 101:210982

REFERENCE 5: 101:130521

REFERENCE 6: 101:130443

REFERENCE 7: 97:127360

REFERENCE 8: 96:34985

REFERENCE 9: 95:219968

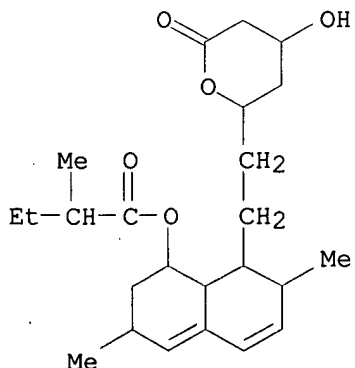
L85 ANSWER 15 OF 40 REGISTRY COPYRIGHT 2001 ACS

RN 79952-43-5 REGISTRY

CN Butanoic acid, 2-methyl-, 1,2,3,7,8,8a-hexahydro-3,7-dimethyl-8-[2-(tetrahydro-4-hydroxy-6-oxo-2H-pyran-2-yl)ethyl]-1-naphthalenyl ester (9CI) (CA INDEX NAME)

MF C24 H36 O5

LC STN Files: BEILSTEIN\*, CA, CAPLUS, CHEMINFORMRX, USPATFULL  
(\*File contains numerically searchable property data)



10 REFERENCES IN FILE CA (1967 TO DATE)

10 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 128:140889  
 REFERENCE 2: 113:78161  
 REFERENCE 3: 112:7367  
 REFERENCE 4: 111:133822  
 REFERENCE 5: 101:210982  
 REFERENCE 6: 101:130521  
 REFERENCE 7: 101:130443  
 REFERENCE 8: 99:70288  
 REFERENCE 9: 96:34985  
 REFERENCE 10: 95:219968

L85 ANSWER 16 OF 40 REGISTRY COPYRIGHT 2001 ACS

RN 79902-41-3 REGISTRY

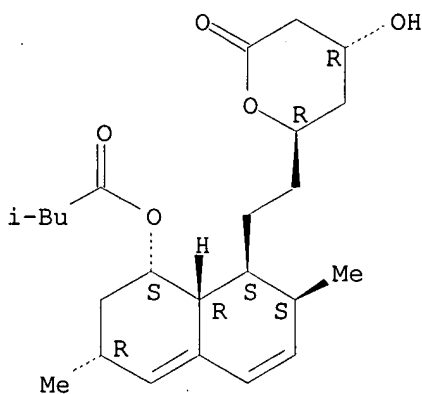
CN Butanoic acid, 3-methyl-, 1,2,3,7,8,8a-hexahydro-3,7-dimethyl-8-[2-(tetrahydro-4-hydroxy-6-oxo-2H-pyran-2-yl)ethyl]-1-naphthalenyl ester, [1S-[1.alpha.,3.alpha.,7.beta.,8.beta.(2S\*,4S\*),8a.beta.]]- (9CI)  
 (CA INDEX NAME)

FS STEREOSEARCH

MF C24 H36 O5

LC STN Files: BEILSTEIN\*, CA, CAPLUS, CASREACT, TOXLIT, USPATFULL  
 (\*File contains numerically searchable property data)

Absolute stereochemistry.



7 REFERENCES IN FILE CA (1967 TO DATE)  
 7 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 122:263678  
 REFERENCE 2: 110:18101  
 REFERENCE 3: 104:186228  
 REFERENCE 4: 101:210982  
 REFERENCE 5: 101:130521  
 REFERENCE 6: 96:34985  
 REFERENCE 7: 95:219968

L85 ANSWER 17 OF 40 REGISTRY COPYRIGHT 2001 ACS

RN 75330-75-5 REGISTRY

CN Butanoic acid, 2-methyl-, (1S,3R,7S,8S,8aR)-1,2,3,7,8,8a-hexahydro-3,7-dimethyl-8-[2-[(2R,4R)-tetrahydro-4-hydroxy-6-oxo-2H-pyran-2-yl]ethyl]-1-naphthalenyl ester, (2S)- (9CI) (CA INDEX NAME)

OTHER CA INDEX NAMES:

CN Butanoic acid, 2-methyl-, 1,2,3,7,8,8a-hexahydro-3,7-dimethyl-8-[2-(tetrahydro-4-hydroxy-6-oxo-2H-pyran-2-yl)ethyl]-1-naphthalenyl ester, [1S-[1.alpha.(R\*),3.alpha.,7.beta.,8.beta.(2S\*,4S\*),8a.beta.]]-

OTHER NAMES:

CN (+)-Mevinolin

CN Antibiotic MB 530B

CN L 154803

CN Lovastatin

CN Mevacor

CN Mevinolin

CN MK 803

CN Monacolin K

CN Monacolin K lactone

CN MSD 803

FS STEREOSEARCH

DR 71949-96-7, 74133-25-8, 81739-26-6

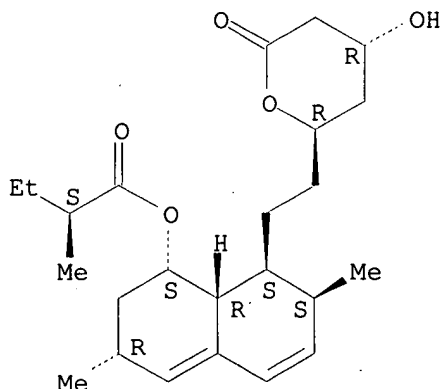
MF C24 H36 O5

CI COM

LC STN Files: AGRICOLA, AIDSLINE, ANABSTR, BEILSTEIN\*, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CANCERLIT, CAPLUS, CASREACT, CBNB, CEN, CHEMCATS, CHEMINFORMRX, CHEMLIST, CIN, CSCHEM, CSNB, DDFU, DIOGENES, DRUGNL, DRUGPAT, DRUGU, DRUGUPDATES, EMBASE, HSDB\*, IFICDB, IFIUDB, IMSDIRECTORY, IPA, MEDLINE, MRCK\*, MSDS-OHS, NAPRALERT, NIOSHTIC, PHAR, PROMT, RTECS\*, SPECINFO, SYNTHLINE, TOXLINE, TOXLIT, USAN, USPATFULL  
(\*File contains numerically searchable property data)

Other Sources: WHO

Absolute stereochemistry.



1330 REFERENCES IN FILE CA (1967 TO DATE)

50 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA

1331 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 135:10035

REFERENCE 2: 135:2587

REFERENCE 3: 135:364

REFERENCE 4: 135:363

REFERENCE 5: 134:371882

REFERENCE 6: 134:365738

REFERENCE 7: 134:362292

REFERENCE 8: 134:361140

REFERENCE 9: 134:361049

REFERENCE 10: 134:357587

L85 ANSWER 18 OF 40 REGISTRY COPYRIGHT 2001 ACS

RN 75225-51-3 REGISTRY

CN 1-Naphthaleneheptanoic acid, 1,2,6,7,8,8a-hexahydro-.beta.,.delta.-  
dihydroxy-2,6-dimethyl-8-[(2S)-2-methyl-1-oxobutoxy]-,  
(.beta.R,.delta.R,1S,2S,6R,8S,8aR)- (9CI) (CA INDEX NAME)

OTHER CA INDEX NAMES:

CN 1-Naphthaleneheptanoic acid, 1,2,6,7,8,8a-hexahydro-.beta.,.delta.-  
dihydroxy-2,6-dimethyl-8-(2-methyl-1-oxobutoxy)-, [1S-  
[1.alpha.(.beta.S\*,.delta.S\*),2.alpha.,6.beta.,8.beta.(R\*),8a.alpha.]]-

OTHER NAMES:

CN L 154819

CN Lovastatin acid

CN Mevinolinic acid

CN MK 819

CN Monacolinic K acid

CN MSD 803 acid

CN MSD 803 free acid

FS STEREOSEARCH

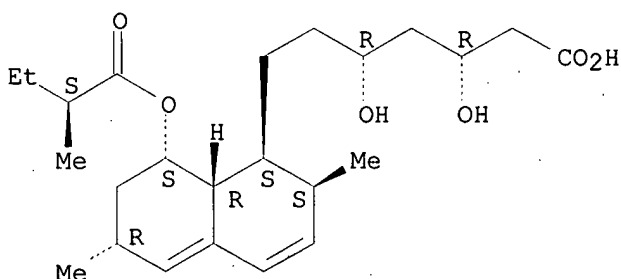
DR 76556-02-0, 77285-87-1

MF C24 H38 O6

CI COM

LC STN Files: AGRICOLA, ANABSTR, BEILSTEIN\*, BIOBUSINESS, BIOSIS,  
BIOTECHNO, CA, CAPLUS, DDFU, DRUGU, EMBASE, IPA, MEDLINE, NAPRALERT,  
RTECS\*, TOXLINE, TOXLIT, USPATFULL  
(\*File contains numerically searchable property data)

Absolute stereochemistry.



72 REFERENCES IN FILE CA (1967 TO DATE)

7 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA

72 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 134:336227

REFERENCE 2: 134:325321

REFERENCE 3: 134:304920

REFERENCE 4: 134:275767

REFERENCE 5: 134:188026

REFERENCE 6: 133:3757

REFERENCE 7: 132:278495

REFERENCE 8: 132:278494

REFERENCE 9: 132:241979

REFERENCE 10: 132:202648

L85 ANSWER 19 OF 40 REGISTRY COPYRIGHT 2001 ACS

RN 71806-22-9 REGISTRY

CN Tryptophan, N-[(9Z)-1-oxo-9-octadecenyl]-, ethyl ester (9CI) (CA INDEX NAME)

OTHER CA INDEX NAMES:

CN DL-Tryptophan, N-(1-oxo-9-octadecenyl)-, ethyl ester, (Z)-

OTHER NAMES:

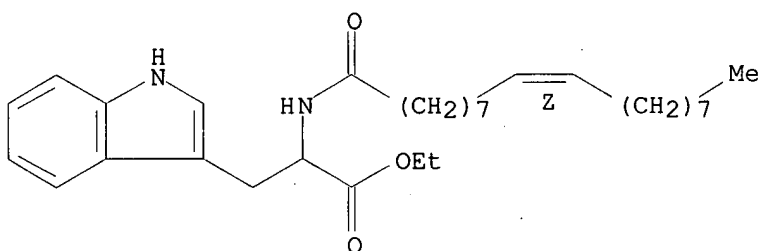
CN Tryptophan, N-(1-oxo-9-octadecenyl)-, ethyl ester, (Z)-

FS STEREOSEARCH

MF C31 H48 N2 O3

LC STN Files: BEILSTEIN\*, CA, CAPLUS, CHEMCATS, MEDLINE, TOXLIT, USPATFULL  
(\*File contains numerically searchable property data)

Double bond geometry as shown.



6 REFERENCES IN FILE CA (1967 TO DATE)

6 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 129:402

REFERENCE 2: 102:89686

REFERENCE 3: 101:152341

REFERENCE 4: 100:45116

REFERENCE 5: 94:174880

REFERENCE 6: 91:193639

L85 ANSWER 20 OF 40 REGISTRY COPYRIGHT 2001 ACS

RN 65589-58-4 REGISTRY

CN Agar, hydrogen sulfate (9CI) (CA INDEX NAME)

MF H2 O4 S . x Unspecified

PCT Manual registration

LC STN Files: CA, CAPLUS, CHEMLIST, TOXLIT, USPATFULL

Other Sources: EINECS\*\*

(\*\*Enter CHEMLIST File for up-to-date regulatory information)

CM 1

CRN 9002-18-0

CMF Unspecified

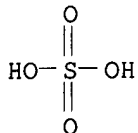
CCI PMS, MAN

\*\*\* STRUCTURE DIAGRAM IS NOT AVAILABLE \*\*\*

CM 2

CRN 7664-93-9

CMF H2 O4 S



6 REFERENCES IN FILE CA (1967 TO DATE)

6 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 126:297659

REFERENCE 2: 103:179896

REFERENCE 3: 103:179895

REFERENCE 4: 92:15572

REFERENCE 5: 88:146096

REFERENCE 6: 88:83512

L85 ANSWER 21 OF 40 REGISTRY COPYRIGHT 2001 ACS

RN 37293-26-8 REGISTRY

CN Chitosan, hydrogen sulfate (ester) (9CI) (CA INDEX NAME)

OTHER NAMES:

CN Chitosan polysulfate

CN Chitosan sulfate

MF H2 O4 S . x Unspecified

CI COM

PCT Manual registration

LC STN Files: BIOSIS, CA, CAPLUS, DDFU, DRUGU, IFICDB, IFIPAT, IFIUDB,  
PIRA, PROMT, TOXLIT, USPATFULL

CM 1

CRN 9012-76-4

CMF Unspecified

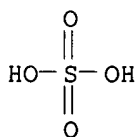
CCI PMS, MAN

\*\*\* STRUCTURE DIAGRAM IS NOT AVAILABLE \*\*\*

CM 2

CRN 7664-93-9

CMF H2 O4 S



71 REFERENCES IN FILE CA (1967 TO DATE)

8 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA

71 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 134:168390  
REFERENCE 2: 133:297783  
REFERENCE 3: 133:168289  
REFERENCE 4: 133:147274  
REFERENCE 5: 132:284193  
REFERENCE 6: 132:207622  
REFERENCE 7: 131:314156  
REFERENCE 8: 131:311873  
REFERENCE 9: 131:233584  
REFERENCE 10: 131:63497

L85 ANSWER 22 OF 40 REGISTRY COPYRIGHT 2001 ACS

RN 9049-31-4 REGISTRY

CN Alginic acid, hydrogen sulfate (9CI) (CA INDEX NAME)

OTHER NAMES:

CN Algin sulfate

CN Alginic acid sulfate

MF H2 O4 S . x Unspecified

CI COM

PCT Manual registration

LC STN Files: BIOSIS, CA, CAPLUS, NAPRALERT, TOXLIT, USPATFULL

CM 1

CRN 9005-32-7

CMF Unspecified

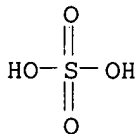
CCI PMS, MAN

\*\*\* STRUCTURE DIAGRAM IS NOT AVAILABLE \*\*\*

CM 2

CRN 7664-93-9

CMF H2 O4 S



22 REFERENCES IN FILE CA (1967 TO DATE)

2 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA

22 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 133:155175  
REFERENCE 2: 133:147274  
REFERENCE 3: 129:2249  
REFERENCE 4: 128:317217  
REFERENCE 5: 126:297659

REFERENCE 6: 125:76389  
REFERENCE 7: 122:222702  
REFERENCE 8: 121:91354  
REFERENCE 9: 120:95787  
REFERENCE 10: 117:257993

L85 ANSWER 23 OF 40 REGISTRY COPYRIGHT 2001 ACS  
RN 9047-13-6 REGISTRY  
CN Amylopectin, hydrogen sulfate (9CI) (CA INDEX NAME)  
OTHER NAMES:  
CN Amylopectin sulfate  
CN Sulfated amylopectin  
MF H2 O4 S . x Unspecified  
PCT Manual registration  
LC STN Files: BIOSIS, CA, CANCERLIT, CAPLUS, EMBASE, MEDLINE, RTECS\*,  
TOXLINE, TOXLIT, USPATFULL  
(\*File contains numerically searchable property data)

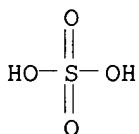
CM 1

CRN 9037-22-3  
CMF Unspecified  
CCI PMS, MAN

\*\*\* STRUCTURE DIAGRAM IS NOT AVAILABLE \*\*\*

CM 2

CRN 7664-93-9  
CMF H2 O4 S



33 REFERENCES IN FILE CA (1967 TO DATE)  
3 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA  
33 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 126:297659  
REFERENCE 2: 125:109645  
REFERENCE 3: 121:6622  
REFERENCE 4: 119:133233  
REFERENCE 5: 116:99057  
REFERENCE 6: 111:739  
REFERENCE 7: 106:190869  
REFERENCE 8: 103:64471  
REFERENCE 9: 102:110545  
REFERENCE 10: 99:124377



L85 ANSWER 24 OF 40 REGISTRY COPYRIGHT 2001 ACS  
RN 9042-14-2 REGISTRY  
CN Dextran, hydrogen sulfate (9CI) (CA INDEX NAME)  
OTHER NAMES:  
CN Dextran polysulfate  
CN Dextran sulfate  
CN Dextran sulfate 500  
CN Dextran sulfate 5000  
CN Dextran sulfuric acid  
CN Dextran sulphate  
CN MDS-Kowa  
CN NSC 620255  
CN PF 51  
CN PF 51 (carbohydrate)  
CN Polydextran sulfate  
CN Polyglucin, sulfate  
CN Sulfopolyglucin  
CN T 500  
DR 9057-27-6, 9063-02-9, 50935-34-7, 37271-05-9, 73075-68-0, 191288-77-4  
MF H2 O4 S . x Unspecified  
CI COM  
PCT Manual registration, Polyother, Polyother only  
LC STN Files: ADISINSIGHT, AGRICOLA, AIDSLINE, ANABSTR, BIOBUSINESS,  
BIOSIS, BIOTECHNO, CA, CANCERLIT, CAPLUS, CBNB, CEN, CHEMCATS, CHEMLIST,  
CIN, CSCHEM, DDFU, DRUGU, EMBASE, IFICDB, IFIPAT, IFIUDB, IPA, MEDLINE,  
NIOSHTIC, PIRA, PROMT, RTECS\*, TOXLINE, TOXLIT, USAN, USPATFULL, VTB  
(\*File contains numerically searchable property data)  
Other Sources: NDSL\*\*, TSCA\*\*  
(\*\*Enter CHEMLIST File for up-to-date regulatory information)

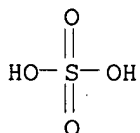
CM 1

CRN 9004-54-0  
CMF Unspecified  
CCI PMS, MAN

\*\*\* STRUCTURE DIAGRAM IS NOT AVAILABLE \*\*\*

CM 2

CRN 7664-93-9  
CMF H2 O4 S



2331 REFERENCES IN FILE CA (1967 TO DATE)  
155 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA  
2331 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 135:10087  
REFERENCE 2: 135:4580  
REFERENCE 3: 135:2524  
REFERENCE 4: 135:485  
REFERENCE 5: 134:361390

REFERENCE 6: 134:331616

REFERENCE 7: 134:325204

REFERENCE 8: 134:322477

REFERENCE 9: 134:320868

REFERENCE 10: 134:316194

L85 ANSWER 25 OF 40 REGISTRY COPYRIGHT 2001 ACS

RN 9037-22-3 REGISTRY

CN Amylopectin (9CI) (CA INDEX NAME)

OTHER NAMES:

CN Amaizo 839

CN Amioca

CN Amioca WCS

CN C\*Pharm 12018

CN Cato 225

CN Cato 240

CN Cato 270

CN Farinex WM 85

CN Film Kote 54

CN Honen Alpha Waxy Starch

CN Kosol

CN Pectin, amylo

CN Starch, waxy

CN Ultraamylopectin N

CN Ultrasperse A

CN Waxy 7350

CN Waxy corn starch

CN Waxy maize starch

CN Waxy starch

CN WCS

DR 9050-86-6, 189047-96-9

MF Unspecified

CI PMS, COM, MAN

PCT Manual registration, Polyother, Polyother only

LC STN Files: AGRICOLA, AIDSLINE, ANABSTR, BIOBUSINESS, BIOSIS, BIOTECHNO,  
CA, CABA, CANCERLIT, CAPLUS, CASREACT, CBNB, CEN, CHEMCATS, CHEMLIST,  
CIN, CSCHEM, DDFU, DRUGU, EMBASE, IFICDB, IFIPAT, IFIUDB, IPA, MEDLINE,  
MRCK\*, NAPRALERT, PIRA, PROMT, TOXLINE, TOXLIT, TULSA, USPATFULL

(\*File contains numerically searchable property data)

Other Sources: DSL\*\*, EINECS\*\*, TSCA\*\*

(\*\*Enter CHEMLIST File for up-to-date regulatory information)

\*\*\* STRUCTURE DIAGRAM IS NOT AVAILABLE \*\*\*

2428 REFERENCES IN FILE CA (1967 TO DATE)

182 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA

2431 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 135:3149

REFERENCE 2: 134:365927

REFERENCE 3: 134:365921

REFERENCE 4: 134:354771

REFERENCE 5: 134:354765

REFERENCE 6: 134:352542

REFERENCE 7: 134:352532

REFERENCE 8: 134:339847

REFERENCE 9: 134:339804

REFERENCE 10: 134:337490

L85 ANSWER 26 OF 40 REGISTRY COPYRIGHT 2001 ACS

RN 9032-43-3 REGISTRY

CN Cellulose, hydrogen sulfate (9CI) (CA INDEX NAME)

OTHER NAMES:

CN Cellulose sulfate

CN Sulfate cellulose

CN Sulfo cellulose

DR 166736-01-2, 55187-33-2

MF H2 O4 S . x Unspecified

CI COM

PCT Manual registration

LC STN Files: AGRICOLA, ANABSTR, BIOBUSINESS, BIOSIS, BIOTECHNO, CA,  
CANCERLIT, CAPLUS, CBNB, CIN, DDFU, DRUGU, EMBASE, IFICDB, IFIPAT,  
IFIUDB, MEDLINE, PIRA, PROMT, TOXLINE, TOXLIT, TULSA, USPATFULL

CM 1

CRN 9004-34-6

CMF Unspecified

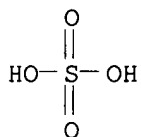
CCI PMS, MAN

\*\*\* STRUCTURE DIAGRAM IS NOT AVAILABLE \*\*\*

CM 2

CRN 7664-93-9

CMF H2 O4 S



401 REFERENCES IN FILE CA (1967 TO DATE)

46 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA

401 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 135:4580

REFERENCE 2: 134:174523

REFERENCE 3: 134:163843

REFERENCE 4: 134:117314

REFERENCE 5: 134:73167

REFERENCE 6: 134:44011

REFERENCE 7: 133:340251

REFERENCE 8: 133:305579

REFERENCE 9: 133:283174

REFERENCE 10: 133:271421

L85 ANSWER 27 OF 40 REGISTRY COPYRIGHT 2001 ACS

RN 9027-63-8 REGISTRY  
CN Acyltransferase, cholesterol (9CI) (CA INDEX NAME)  
OTHER NAMES:  
CN ACAT  
CN Acyl coenzyme A-cholesterol O-acyltransferase  
CN Acyl-CoA:cholesteryl acyltransferase  
CN Acyl-coenzyme A-sterol acyltransferase  
CN Acyl-coenzyme A:cholesterol acyltransferase  
CN AcylCoA-Cholesterol acyltransferase  
CN AcylCoA-cholesterol O-acyltransferase  
CN Cholesterol acyltransferase  
CN Cholesterol ester synthase  
CN Cholesterol ester synthetase  
CN Cholesteryl ester synthetase  
CN E.C. 2.3.1.26  
CN Steryl ester synthase  
MF Unspecified  
CI MAN  
LC STN Files: AGRICOLA, ANABSTR, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CABA,  
CAPLUS, CBNB, CEN, CIN, EMBASE, PROMT, TOXLIT, USPATFULL

\*\*\* STRUCTURE DIAGRAM IS NOT AVAILABLE \*\*\*

1482 REFERENCES IN FILE CA (1967 TO DATE)

2 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA

1482 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 135:3664  
REFERENCE 2: 135:1241  
REFERENCE 3: 135:369  
REFERENCE 4: 134:371771  
REFERENCE 5: 134:338258  
REFERENCE 6: 134:337498  
REFERENCE 7: 134:323882  
REFERENCE 8: 134:323687  
REFERENCE 9: 134:321178  
REFERENCE 10: 134:311218

L85 ANSWER 28 OF 40 REGISTRY COPYRIGHT 2001 ACS

RN 9026-00-0 REGISTRY  
CN Esterase, cholesterol (9CI) (CA INDEX NAME)  
OTHER NAMES:  
CN Cholesterase  
CN Cholesterin esterase  
CN Cholesterol ester hydrolase  
CN Cholesterol esterase  
CN Cholesteryl ester hydrolase  
CN Cholesteryl esterase  
CN E.C. 3.1.1.13  
CN Lysosomal acid lipase  
CN Neutral cholesteryl ester hydrolase  
CN Sterol ester hydrolase  
CN Sterol esterase  
DR 9040-56-6  
MF Unspecified  
CI MAN  
LC STN Files: AGRICOLA, ANABSTR, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CABA,  
CAPLUS, CASREACT, CHEMCATS, CHEMINFORMRX, CHEMLIST, CIN, CSCHEM, EMBASE,

IFICDB, IFIPAT, IFIUDB, PROMT, TOXLIT, USPATFULL  
Other Sources: EINECS\*\*, TSCA\*\*  
(\*\*Enter CHEMLIST File for up-to-date regulatory information)

\*\*\* STRUCTURE DIAGRAM IS NOT AVAILABLE \*\*\*

1552 REFERENCES IN FILE CA (1967 TO DATE)

21 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA

1552 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 135:1241  
REFERENCE 2: 134:362292  
REFERENCE 3: 134:353586  
REFERENCE 4: 134:350257  
REFERENCE 5: 134:348257  
REFERENCE 6: 134:323855  
REFERENCE 7: 134:320830  
REFERENCE 8: 134:292266  
REFERENCE 9: 134:249944  
REFERENCE 10: 134:249194

L85 ANSWER 29 OF 40 REGISTRY COPYRIGHT 2001 ACS

RN 9012-77-5 REGISTRY

CN Pectin, hydrogen sulfate (9CI) (CA INDEX NAME)

OTHER NAMES:

CN Pectin polysulfate

DR 37221-19-5

MF H2 O4 S . x Unspecified

CI COM

PCT Manual registration

LC STN Files: CA, CAPLUS, IFICDB, IFIPAT, IFIUDB, TOXLIT, USPATFULL

CM 1

CRN 9000-69-5

CMF Unspecified

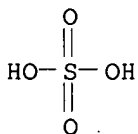
CCI PMS, MAN

\*\*\* STRUCTURE DIAGRAM IS NOT AVAILABLE \*\*\*

CM 2

CRN 7664-93-9

CMF H2 O4 S



7 REFERENCES IN FILE CA (1967 TO DATE)

7 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 133:147274

REFERENCE 2: 126:297659

REFERENCE 3: 83:12708

REFERENCE 4: 82:103170

REFERENCE 5: 79:20613

REFERENCE 6: 78:126096

REFERENCE 7: 77:77034

L85 ANSWER 30 OF 40 REGISTRY COPYRIGHT 2001 ACS

RN 9012-76-4 REGISTRY

CN Chitosan (8CI, 9CI) (CA INDEX NAME)

OTHER NAMES:

CN 100D-VL

CN Biopolymer L 112

CN Chicol

CN Chitan, N-acetyl-

CN Chitin, N-deacetyl-

CN Chitofine

CN Chitoparl 3510

CN Chitoparl BC 3000

CN Chitoparl BCW 2500

CN Chitoparl BCW 3000

CN Chitoparl BCW 3500

CN Chitoparl BCW 3505

CN Chitoparl BCW 3507

CN Chitosan 500

CN Chitosan CLH

CN Chitosan EL

CN Chitosan F

CN Chitosan FL

CN Chitosan H

CN Chitosan LL

CN Chitosan LL 80

CN Chitosan LLWP

CN Chitosan M

CN Chitosan MP

CN Chitosan SK 10

CN Chitosan VL

CN Chitosom

CN Crystan LA-S

CN CTA 1 Lactic Acid

CN CTA 4

CN DAC 50

CN DAC 70

CN Daichitosan VL

CN Daichitosan W 10

CN Deacetylchitin

CN FCM 117

CN Flonac C

CN Flonac N

CN HC 1

CN HC 1 (polysaccharide)

CN Hiset KW 5

CN Hydagen CMFP

CN Hydagen HCMF

CN Kimitsu Chitosan F

CN Kimitsu Chitosan F 2

CN Kimitsu Chitosan F 2P

CN Kimitsu Chitosan H

CN Kimitsu Chitosan L

CN Kimitsu Chitosan LL

CN Kimitsu Chitosan LLW

ADDITIONAL NAMES NOT AVAILABLE IN THIS FORMAT - Use FCN, FIDE, or ALL for  
DISPLAY

DR 57285-05-9

MF Unspecified

CI PMS, COM, MAN

PCT Manual registration, Polyother, Polyother only

LC STN Files: AGRICOLA, AIDSLINE, ANABSTR, BIOBUSINESS, BIOSIS, BIOTECHNO,  
CA, CABA, CANCERLIT, CAPLUS, CASREACT, CBNB, CEN, CHEMCATS, CHEMLIST,  
CIN, CSCHEM, DDFU, DIOGENES, DRUGU, EMBASE, IFICDB, IFIPAT, IFIUIDB, IPA,  
MEDLINE, NAPRALERT, PHAR, PIRA, PROMT, RTECS\*, TOXLINE, TOXLIT, TULSA,  
USAN, USPATFULL, VTB

(\*File contains numerically searchable property data)

Other Sources: NDSL\*\*, TSCA\*\*, WHO

(\*\*Enter CHEMLIST File for up-to-date regulatory information)

\*\*\* STRUCTURE DIAGRAM IS NOT AVAILABLE \*\*\*

8810 REFERENCES IN FILE CA (1967 TO DATE)

1695 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA

8835 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 135:10087

REFERENCE 2: 135:10066

REFERENCE 3: 135:10022

REFERENCE 4: 135:9998

REFERENCE 5: 135:9941

REFERENCE 6: 135:9907

REFERENCE 7: 135:9880

REFERENCE 8: 135:9398

REFERENCE 9: 135:9395

REFERENCE 10: 135:9376

L85 ANSWER 31 OF 40 REGISTRY COPYRIGHT 2001 ACS

RN 9005-49-6 REGISTRY

CN Heparin (8CI, 9CI) (CA INDEX NAME)

OTHER NAMES:

CN .alpha.-Heparin

CN Bemiparin

CN Certoparin

CN Clexane

CN Clivarin

CN Clivarine

CN CY 216

CN CY 222

CN Dalteparin

CN Enoxaparin

CN Fluxum

CN FR 860

CN Fragmin A

CN Fragmin B

CN Fraxiparin

CN Heparin sulfate

CN Heparinic acid

CN KB 101

CN Multiparin

CN Novoheparin

CN OP 386

CN OP 622

CN Pabyrn  
CN Parnaparin  
CN Parvoparin  
CN Reviparin  
CN Sandoparin  
CN Sublingula  
CN Vetren  
CN Vitrum AB  
DR 9075-96-1, 11078-24-3, 11129-39-8, 104521-37-1, 37324-73-5, 91449-79-5  
MF Unspecified  
CI PMS, COM, MAN  
PCT Manual registration, Polyester, Polyester formed  
LC STN Files: AGRICOLA, AIDSLINE, ANABSTR, BIOBUSINESS, BIOSIS, BIOTECHNO,  
CA, CABA, CANCERLIT, CAPLUS, CASREACT, CBNB, CEN, CHEMCATS, CHEMLIST,  
CIN, CSCHEM, DDFU, DIOGENES, DRUGNL, DRUGPAT, DRUGU, DRUGUPDATES,  
EMBASE, HSDB\*, IFICDB, IFIPAT, IFIUDB, IMSDIRECTORY, IPA, MEDLINE,  
MRCK\*, MSDS-OHS, NAPRALERT, NIOSHTIC, PHAR, PIRA, PROMT, RTECS\*,  
TOXLINE, TOXLIT, USAN, USPATFULL  
(\*File contains numerically searchable property data)  
Other Sources: DSL\*\*, EINECS\*\*, WHO  
(\*\*Enter CHEMLIST File for up-to-date regulatory information)

\*\*\* STRUCTURE DIAGRAM IS NOT AVAILABLE \*\*\*

17089 REFERENCES IN FILE CA (1967 TO DATE)

1710 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA

17101 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 135:10062

REFERENCE 2: 135:10016

REFERENCE 3: 135:2500

REFERENCE 4: 135:1998

REFERENCE 5: 135:1890

REFERENCE 6: 135:485

REFERENCE 7: 135:342

REFERENCE 8: 135:303

REFERENCE 9: 135:298

REFERENCE 10: 135:291

L85 ANSWER 32 OF 40 REGISTRY COPYRIGHT 2001 ACS

RN 9005-38-3 REGISTRY

CN Alginic acid, sodium salt (8CI, 9CI) (CA INDEX NAME)

OTHER NAMES:

CN 1-3F

CN A 7C618

CN Algin

CN Algin (polysaccharide)

CN Algin ML

CN Alginate FD 155

CN Alginate KMF

CN Alginate TBVV/N 2

CN Algipon L 1168

CN Algitex LL

CN Algitex M

CN Algogel HV

CN Algogel LV

CN Algogel MV

CN Algogel MVR



CN Alloid G  
CN Amnucol  
CN Antimigrant C 45  
CN Cecalgin HV 600  
CN Cecalgin HV/KL 600  
CN Cecalgine TBV  
CN CHT Alginate EHV  
CN CHT Alginate MV  
CN Cohasal IH  
CN Darid QH  
CN Dariloid QH  
CN Dialgin HV  
CN Duck Algin  
CN Duck Algin EX 30  
CN Duck Algin NSPH  
CN Duck Algin NSPL  
CN Duck Algin NSPLL  
CN Duck Algin NSPM  
CN Duck Algin S  
CN EHV  
CN Halltex  
CN IL 2  
CN Kelco Gel HV  
CN Kelco Gel LV  
CN Kelcosol  
CN Kelgin  
CN Kelgin F  
CN Kelgin HV  
CN Kelgin LV  
CN Kelgin MV  
CN Kelgin QH  
CN Kelgin QM  
CN Kelgin RL  
CN Kelgin XL  
CN Kelp Algin L

ADDITIONAL NAMES NOT AVAILABLE IN THIS FORMAT - Use FCN, FIDE, or ALL for  
DISPLAY

DR 12772-46-2, 9005-40-7, 56940-21-7, 56940-22-8, 63278-91-1, 50643-02-2,  
77030-65-0, 81989-21-1, 32129-82-1, 32197-42-5

MF Unspecified

CI PMS, COM, MAN

PCT Manual registration, Polyester, Polyester formed

LC STN Files: AGRICOLA, ANABSTR, BIOBUSINESS, BIOSIS, BIOTECHNO, CA,  
CAPLUS, CASREACT, CBNB, CEN, CHEMCATS, CHEMLIST, CIN, CSCHEM, DETHERM\*,  
DIOGENES, EMBASE, HSDB\*, IFICDB, IFIPAT, IFIUDB, IMSDIRECTORY, IPA,  
MRCK\*, MSDS-OHS, NAPRALERT, NIOSHTIC, PIRA, PROMT, RTECS\*, TOXLINE,  
TOXLIT, TULSA, USAN, USPATFULL, VTB

(\*File contains numerically searchable property data)

Other Sources: DSL\*\*, TSCA\*\*

(\*\*Enter CHEMLIST File for up-to-date regulatory information)

\*\*\* STRUCTURE DIAGRAM IS NOT AVAILABLE \*\*\*

6571 REFERENCES IN FILE CA (1967 TO DATE)

154 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA

6575 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 135:10016

REFERENCE 2: 135:9786

REFERENCE 3: 135:4871

REFERENCE 4: 135:4734

REFERENCE 5: 135:2848

REFERENCE 6: 134:373026

REFERENCE 7: 134:371799

REFERENCE 8: 134:371776

REFERENCE 9: 134:371718

REFERENCE 10: 134:368947

L85 ANSWER 33 OF 40 REGISTRY COPYRIGHT 2001 ACS

RN 9005-32-7 REGISTRY

CN Alginic acid (8CI, 9CI) (CA INDEX NAME)

OTHER NAMES:

CN A 2830-9

CN Acid Algin G 2

CN Kelacid

CN Landalgine

CN Nörgine

CN Protanal LF

CN Satialgine-H 8

CN Snow acid algin G

CN Verdyol Super

DR 210888-24-7

MF Unspecified

CI PMS, COM, MAN

PCT Manual registration, Polyester, Polyester formed

LC STN Files: AGRICOLA, ANABSTR, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CABA, CANCERLIT, CAPLUS, CASREACT, CBNB, CHEMCATS, CHEMLIST, CHEMSAFE, CIN, CSCHEM, DDFU, DIOGENES, DRUGU, EMBASE, HSDB\*, IFICDB, IFIPAT, IFIUDB, IPA, MEDLINE, MRCK\*, MSDS-OHS, NAPRALERT, NIOSHTIC, PIRA, PROMT, RTECS\*, TOXLINE, TOXLIT, USAN, USPATFULL

(\*File contains numerically searchable property data)

Other Sources: DSL\*\*, EINECS\*\*, TSCA\*\*

(\*\*Enter CHEMLIST File for up-to-date regulatory information)

\*\*\* STRUCTURE DIAGRAM IS NOT AVAILABLE \*\*\*

5047 REFERENCES IN FILE CA (1967 TO DATE)

1188 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA

5052 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 135:10038

REFERENCE 2: 135:9786

REFERENCE 3: 135:7315

REFERENCE 4: 135:7198

REFERENCE 5: 135:7186

REFERENCE 6: 135:4828

REFERENCE 7: 135:4565

REFERENCE 8: 135:2523

REFERENCE 9: 135:1638

REFERENCE 10: 134:371859

L85 ANSWER 34 OF 40 REGISTRY COPYRIGHT 2001 ACS

RN 9004-54-0 REGISTRY

CN Dextran (9CI) (CA INDEX NAME)

OTHER CA INDEX NAMES:

CN Dextrans (8CI)

## OTHER NAMES:

CN .alpha.-Dextran  
CN CDC-H  
CN DEX 500  
CN Dextran 1.5  
CN Dextran 10  
CN Dextran 1000  
CN Dextran 110  
CN Dextran 15  
CN Dextran 150  
CN Dextran 2000  
CN Dextran 250  
CN Dextran 3000  
CN Dextran 40  
CN Dextran 45  
CN Dextran 500  
CN Dextran 60  
CN Dextran 70  
CN Dextran 75  
CN Dextran B 512  
CN Dextran B1355  
CN Dextran D 10  
CN Dextran PL 1S  
CN Dextran PT 25  
CN Dextran PVD  
CN Dextran RMI  
CN Dextran T 10  
CN Dextran T 110  
CN Dextran T 150  
CN Dextran T 20  
CN Dextran T 2000  
CN Dextran T 500  
CN Dextran T 70  
CN Dextranen  
CN Dextraven  
CN Eudextran  
CN Expandex  
CN Gentran  
CN Hemodex  
CN Hyscon  
CN Hyskon  
CN Infucoll  
CN Intrader  
CN Intradex  
CN LMD  
CN LMWD  
CN LU 122  
CN LVD  
CN Macrodex  
CN Macrose

ADDITIONAL NAMES NOT AVAILABLE IN THIS FORMAT - Use FCN, FIDE, or ALL for  
DISPLAY

DR 12626-85-6, 9013-80-3, 9044-66-0, 11104-36-2, 11121-03-2, 37224-17-2,  
86280-85-5

MF Unspecified

CI PMS, COM, MAN

PCT Manual registration, Polyother, Polyother only

LC STN Files: AGRICOLA, AIDSLINE, ANABSTR, BIOBUSINESS, BIOSIS, CA, CABA,  
CANCERLIT, CAPLUS, CASREACT, CBNB, CEN, CHEMCATS, CHEMLIST, CIN, CSCHEM,  
DDFU, DETHERM\*, DIOGENES, DRUGU, EMBASE, IFICDB, IFIPAT, IFIUDB,  
IMSDIRECTORY, IPA, MEDLINE, MRCK\*, MSDS-OHS, NIOSHTIC, PHAR, PIRA,  
PROMT, RTECS\*, TOXLINE, TOXLIT, TULSA, USAN, USPATFULL, VTB

(\*File contains numerically searchable property data)

Other Sources: DSL\*\*, EINECS\*\*, TSCA\*\*, WHO

(\*\*Enter CHEMLIST File for up-to-date regulatory information)

\*\*\* STRUCTURE DIAGRAM IS NOT AVAILABLE \*\*\*

10071 REFERENCES IN FILE CA (1967 TO DATE)

1994 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA

10084 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 135:10005

REFERENCE 2: 135:9952

REFERENCE 3: 135:6233

REFERENCE 4: 135:4537

REFERENCE 5: 135:4302

REFERENCE 6: 135:2558

REFERENCE 7: 135:2539

REFERENCE 8: 135:2370

REFERENCE 9: 135:2366

REFERENCE 10: 134:371815

L85 ANSWER 35 OF 40 REGISTRY COPYRIGHT 2001 ACS

RN 9004-34-6 REGISTRY

CN Cellulose (8CI, 9CI) (CA INDEX NAME)

OTHER NAMES:

CN .alpha.-Cellulose

CN .beta.-Amylose

CN 3mAQUACEL

CN 402-2B

CN Alicell LV

CN Alpha Cel PB 25

CN Alphafloc

CN Arbocel

CN Arbocel B 00

CN Arbocel B 600/30

CN Arbocel B 800

CN Arbocel B 820C

CN Arbocel BC 1000

CN Arbocel BC 200

CN Arbocel BE 600

CN Arbocel BE 600/10

CN Arbocel BE 600/20

CN Arbocel BE 600/30

CN Arbocel BWW 40

CN Arbocel DC 1000

CN Arbocel FD 00

CN Arbocel FD 600/30

CN Arbocel FIC 200

CN Arbocel FT 40

CN Arbocel FT 600/30H

CN Arbocel TF 30HG

CN Arbocel TP 40

CN Avicel

CN Avicel 101

CN Avicel 102

CN Avicel 2330

CN Avicel 2331

CN Avicel 955

CN Avicel CL 611

CN Avicel E 200

CN Avicel F 20

CN Avicel FD 100

CN Avicel FD 101  
CN Avicel FD-F 20  
CN Avicel M 06  
CN Avicel M 15  
CN Avicel M 25  
CN Avicel PH 101  
CN Avicel PH 102  
CN Avicel PH 105  
CN Avicel PH 200  
CN Avicel PH 301  
CN Avicel PH 302  
CN Avicel PH-F 10  
CN Avicel PH-F 20

ADDITIONAL NAMES NOT AVAILABLE IN THIS FORMAT - Use FCN, FIDE, or ALL for  
DISPLAY

DR 12656-52-9, 9012-19-5, 9037-50-7, 9076-30-6, 58968-67-5, 99331-82-5,  
67016-75-5, 67016-76-6, 51395-76-7, 61991-21-7, 61991-22-8, 68073-05-2,  
70225-79-5, 74623-16-8, 75398-83-3, 77907-70-1, 84503-75-3, 89468-66-6,  
39394-43-9

MF Unspecified

CI PMS, COM, MAN

PCT Manual registration, Polyother, Polyother only

LC STN Files: AGRICOLA, AIDSLINE, ANABSTR, BIOBUSINESS, BIOSIS, BIOTECHNO,  
CA, CABA, CANCERLIT, CAPLUS, CASREACT, CBNB, CEN, CHEMCATS, CHEMLIST,  
CHEMSAFE, CIN, CSCHEM, CSNB, DDFU, DIOGENES, DRUGU, EMBASE, IFICDB,  
IFIPAT, IFIUDB, IPA, MEDLINE, MRCK\*, MSDS-OHS, NAPRALERT, NIOSHTIC,  
PIRA, PROMT, RTECS\*, TOXLINE, TOXLIT, TULSA, ULIDAT, USAN, USPATFULL,  
VTB

(\*File contains numerically searchable property data)

Other Sources: DSL\*\*, EINECS\*\*, TSCA\*\*

(\*\*Enter CHEMLIST File for up-to-date regulatory information)

\*\*\* STRUCTURE DIAGRAM IS NOT AVAILABLE \*\*\*

52993 REFERENCES IN FILE CA (1967 TO DATE)

6305 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA

53044 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 135:13072

REFERENCE 2: 135:10102

REFERENCE 3: 135:10072

REFERENCE 4: 135:10071

REFERENCE 5: 135:10070

REFERENCE 6: 135:10069

REFERENCE 7: 135:10023

REFERENCE 8: 135:10021

REFERENCE 9: 135:10020

REFERENCE 10: 135:9877

L85 ANSWER 36 OF 40 REGISTRY COPYRIGHT 2001 ACS

RN 9002-18-0 REGISTRY

CN Agar (9CI) (CA INDEX NAME)

OTHER CA INDEX NAMES:

CN Agar-agar (8CI)

OTHER NAMES:

CN Agar Agar Flake

CN Agargel

CN Agaropectin, mixt. with agarose

CN Agarose, mixt. with agarpectin  
CN Bacto-agar  
CN Bengal gelatin  
CN Bengal isinglass  
CN Ceylon isinglass  
CN Chinese isinglass  
CN D 100  
CN D 100 (polysaccharide)  
CN Deltagar LTS  
CN Difco Bacto agar  
CN Digenea simplex mucilage  
CN GAM medium  
CN Gelose  
CN Japan agar  
CN Japan isinglass  
CN Kantennmatsu  
CN Laylor Carang  
CN Luxara 1253  
CN Oxoid III  
CN Oxoid L 11  
CN Phytagar  
CN S 100  
CN S 100 (polysaccharide)  
CN UP 37  
MF Unspecified  
CI PMS, COM, MAN  
PCT Manual registration, Polyother, Polyother only  
LC STN Files: AGRICOLA, AIDSLINE, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CABA,  
CANCERLIT, CAPLUS, CASREACT, CHEMCATS, CHEMLIST, CIN, CSCHEM, DDFU,  
DIOGENES, DRUGU, EMBASE, HSDB\*, IFICDB, IFIPAT, IFIUDB, IPA, MEDLINE,  
MRCK\*, MSDS-OHS, NAPRALERT, NIOSHTIC, PIRA, PROMT, RTECS\*, SPECINFO,  
TOXLINE, TOXLIT, TULSA, USPATFULL  
(\*File contains numerically searchable property data)  
Other Sources: DSL\*\*, EINECS\*\*, TSCA\*\*  
(\*\*Enter CHEMLIST File for up-to-date regulatory information)

\*\*\* STRUCTURE DIAGRAM IS NOT AVAILABLE \*\*\*

3655 REFERENCES IN FILE CA (1967 TO DATE)

76 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA

3658 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 135:4873  
REFERENCE 2: 135:4734  
REFERENCE 3: 135:3035  
REFERENCE 4: 135:2556  
REFERENCE 5: 134:371808  
REFERENCE 6: 134:371776  
REFERENCE 7: 134:366055  
REFERENCE 8: 134:365957  
REFERENCE 9: 134:365838  
REFERENCE 10: 134:364102

L85 ANSWER 37 OF 40 REGISTRY COPYRIGHT 2001 ACS

RN 9000-69-5 REGISTRY

CN Pectin (9CI) (CA INDEX NAME)

OTHER NAMES:

CN AF 701

CN Cesapectin  
CN Colyer pectin  
CN D-D Slowset  
CN Genu JMJ 100  
CN Genu Pectin L 200  
CN Genu Pectin LM 101AS  
CN Genu Pectin LM 104AS  
CN Genu Pectin LM 104AS-FS  
CN Genu Pectin LM 18CG-Z  
CN Genu Pectin X 0905  
CN Genu Pectin YM 100  
CN H&F Pectin Classic AF 701  
CN LM 12CG-Z  
CN LMNA/P 3450NA95  
CN Marpee NL  
CN Marpee OM  
CN Methoxypectin  
CN Methyl pectin  
CN Methyl pectinate  
CN MexPec 1400  
CN Mexpectin XSS 100  
CN Pectin 1694  
CN Pectinate  
CN Pectinic acid  
CN Pectins  
CN Slendid 200  
CN Splendid  
CN Unipectin  
CN Unipectine 3450NA95  
CN Unipectine RS 150.degree. SAG  
CN USP 100  
DR 9046-41-7, 9047-18-1  
MF Unspecified  
CI PMS, COM, MAN  
PCT Manual registration, Polyother, Polyother only  
LC STN Files: AGRICOLA, ANABSTR, BIOBUSINESS, BIOSIS, BIOTECHNO, CA,  
CANCERLIT, CAPLUS, CASREACT, CBNB, CEN, CHEMCATS, CHEMLIST, CIN, CSCHEM,  
DDFU, DIOGENES, DRUGU, EMBASE, HSDB\*, IFICDB, IFIPAT, IFIUDB, IPA,  
MEDLINE, MRCK\*, MSDS-OHS, NAPRALERT, NIOSHTIC, PDLCOM\*, PIRA, PROMT,  
RTECS\*, TOXLINE, TOXLIT, TULSA, USAN, USPATFULL, VTB  
(\*File contains numerically searchable property data)  
Other Sources: DSL\*\*, EINECS\*\*, TSCA\*\*  
(\*\*Enter CHEMLIST File for up-to-date regulatory information)

\*\*\* STRUCTURE DIAGRAM IS NOT AVAILABLE \*\*\*

7478 REFERENCES IN FILE CA (1967 TO DATE)

388 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA

7479 REFERENCES IN FILE CAPLUS (1967 TO DATE)

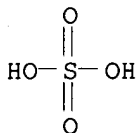
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REFERENCE 2: 135:7092  
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REFERENCE 6: 135:4794  
REFERENCE 7: 135:4710  
REFERENCE 8: 135:4700  
REFERENCE 9: 135:4565

REFERENCE 10: 135:4506

L85 ANSWER 38 OF 40 REGISTRY COPYRIGHT 2001 ACS  
RN 1398-62-5 REGISTRY  
CN Chitin, hydrogen sulfate (ester) (9CI) (CA INDEX NAME)  
OTHER CA INDEX NAMES:  
CN Chitin, sulfate (8CI)  
MF H2 O4 S . x Unspecified  
CI COM  
PCT Manual registration  
LC STN Files: BIOSIS, CA, CAPLUS, TOXLIT, USPATFULL

CM 1

CRN 7664-93-9  
CMF H2 O4 S



CM 2

CRN 1398-61-4  
CMF Unspecified  
CCI MAN

\*\*\* STRUCTURE DIAGRAM IS NOT AVAILABLE \*\*\*

47 REFERENCES IN FILE CA (1967 TO DATE)  
3 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA  
47 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 133:147274

REFERENCE 2: 129:280954

REFERENCE 3: 129:92501

REFERENCE 4: 128:256454

REFERENCE 5: 128:158820

REFERENCE 6: 127:126352

REFERENCE 7: 126:297659

REFERENCE 8: 125:293042

REFERENCE 9: 125:269867

REFERENCE 10: 124:279167

L85 ANSWER 39 OF 40 REGISTRY COPYRIGHT 2001 ACS  
RN 1398-61-4 REGISTRY  
CN Chitin (8CI, 9CI) (CA INDEX NAME)  
OTHER NAMES:  
CN Chitan, N-acetyl-  
CN Chitin Tc-L  
CN Clandosan  
CN Kimitsu Chitin



CN Regitex FA  
DR 9043-70-3, 191802-95-6  
MF Unspecified  
CI COM, MAN  
LC STN Files: AGRICOLA, AIDSLINE, ANABSTR, BIOBUSINESS, BIOSIS, BIOTECHNO,  
CA, CABA, CANCERLIT, CAPLUS, CASREACT, CBNB, CHEMCATS, CHEMLIST, CIN,  
CSCHEM, CSNB, DDFU, DRUGU, EMBASE, IFICDB, IFIPAT, IFIADB, IPA, MEDLINE,  
MRCK\*, NAPRALERT, PROMT, RTECS\*, TOXLINE, TOXLIT, USPATFULL, VETU, VTB  
(\*File contains numerically searchable property data)  
Other Sources: EINECS\*\*, NDSL\*\*, TSCA\*\*  
(\*\*Enter CHEMLIST File for up-to-date regulatory information)

\*\*\* STRUCTURE DIAGRAM IS NOT AVAILABLE \*\*\*

5496 REFERENCES IN FILE CA (1967 TO DATE)

739 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA

5504 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 135:9941  
REFERENCE 2: 135:9810  
REFERENCE 3: 135:7204  
REFERENCE 4: 135:4535  
REFERENCE 5: 135:3074  
REFERENCE 6: 135:2868  
REFERENCE 7: 135:2624  
REFERENCE 8: 135:2192  
REFERENCE 9: 134:366147  
REFERENCE 10: 134:365861

L85 ANSWER 40 OF 40 REGISTRY COPYRIGHT 2001 ACS

RN 57-88-5 REGISTRY

CN Cholest-5-en-3-ol (3.beta.)- (9CI) (CA INDEX NAME)

OTHER CA INDEX NAMES:

CN Cholesterol (8CI)

OTHER NAMES:

CN (-)-Cholesterol

CN .DELTA.5-Cholesten-3.beta.-ol

CN 3.beta.-Hydroxycholest-5-ene

CN 5:6-Cholesten-3.beta.-ol

CN Cholest-5-en-3.beta.-ol

CN Cholesterin

CN Cholesteryl alcohol

CN Dythol

CN Lidinit

CN Lidinite

CN Provitamin D

FS STEREOSEARCH

DR 209124-38-9, 218965-24-3

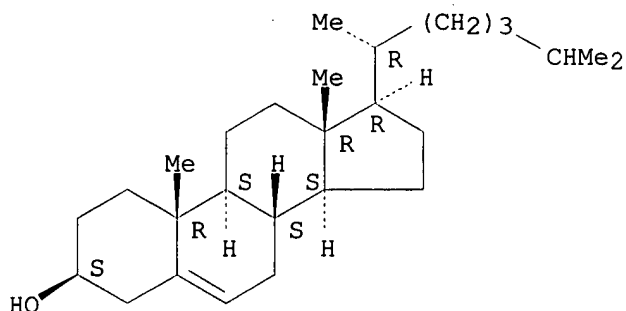
MF C27 H46 O

CI COM

LC STN Files: AGRICOLA, AIDSLINE, ANABSTR, BEILSTEIN\*, BIOBUSINESS, BIOSIS,  
BIOTECHNO, CA, CABA, CANCERLIT, CAOLD, CAPLUS, CASREACT, CBNB, CEN,  
CHEMCATS, CHEMINFORMRX, CHEMLIST, CIN, CSCHEM, CSNB, DDFU, DETHERM\*,  
DIOGENES, DIPPR\*, DRUGU, EMBASE, GMELIN\*, HODOC\*, IFICDB, IFIPAT,  
IFIADB, IPA, MEDLINE, MRCK\*, MSDS-OHS, NAPRALERT, NIOSHTIC, PDLCOM\*,  
PIRA, PROMT, RTECS\*, SPECINFO, TOXLINE, TOXLIT, TULSA, ULIDAT, USAN,  
USPATFULL, VETU, VTB  
(\*File contains numerically searchable property data)

Other Sources: DSL\*\*, EINECS\*\*, TSCA\*\*  
 (\*\*Enter CHEMLIST File for up-to-date regulatory information)

Absolute stereochemistry.



72923 REFERENCES IN FILE CA (1967 TO DATE)  
 7879 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA  
 72997 REFERENCES IN FILE CAPLUS (1967 TO DATE)  
 15 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

REFERENCE 1: 135:13529  
 REFERENCE 2: 135:9934  
 REFERENCE 3: 135:9933  
 REFERENCE 4: 135:5228  
 REFERENCE 5: 135:4955  
 REFERENCE 6: 135:4954  
 REFERENCE 7: 135:4944  
 REFERENCE 8: 135:4943  
 REFERENCE 9: 135:4938  
 REFERENCE 10: 135:4934

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FILE COVERS 1947 - 23 Jun 2001 VOL 135 ISS 1  
 FILE LAST UPDATED: 22 Jun 2001 (20010622/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

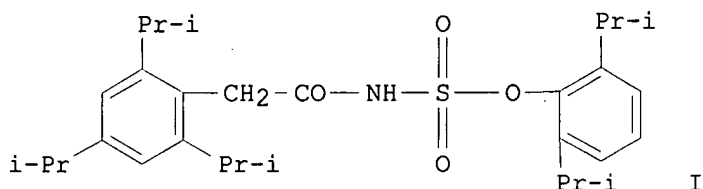
This file supports REGISTRY for direct browsing and searching of all substance data from the REGISTRY file. Enter HELP FIRST for more information.

HCAplus now provides online access to patents and literature covered in CA from 1947 to the present. On April 22, 2001, bibliographic information and abstracts were added for over 2.2 million references published in CA from 1947 to 1966.

=> d 183 bib abs hitrn tot

L83 ANSWER 1 OF 13 HCAPLUS COPYRIGHT 2001 ACS  
 AN 2001:359777 HCAPLUS  
 DN 134:371771  
 TI Prevention of plaque rupture by **ACAT** inhibitors  
 IN Bocan, Thomas Michael Andrew  
 PA Warner-Lambert Company, USA  
 SO PCT Int. Appl., 108 pp.  
 CODEN: PIXXD2  
 DT Patent  
 LA English  
 FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2001034127	A1	20010517	WO 2000-US28705	20001017
	W:				
	AE, AG, AL, AU, BA, BB, BG, BR, BZ, CA, CN, CR, CU, CZ, DM, DZ, EE, GD, GE, HR, HU, ID, IL, IN, IS, JP, KP, KR, LC, LK, LR, LT, LV, MA, MG, MK, MN, MX, MZ, NO, NZ, PL, RO, SG, SI, SK, SL, TR, TT, UA, US, UZ, VN, YU, ZA, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW:				
	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
PRAI	US 1999-163814	P	19991105		
GI					



AB This invention is the administration of an **ACAT** inhibitor to prevent monocyte-macrophage accumulation and MMP expression in atherosclerotic lesions. Further, this invention relates to methods of inhibiting destabilization and/or rupture of atherosclerotic plaques and treatment of unstable angina. Tablets were prepd. contg. a **ACAT** inhibitor such as I.

IT 9027-63-8, Acyl coenzyme A-cholesterol  
**acyltransferase**

RL: BSU (Biological study, unclassified); BIOL (Biological study)  
 (inhibitors; prevention of plaque rupture by **ACAT** inhibitors)

IT 202401-34-1

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (prevention of plaque rupture by **ACAT** inhibitors)

RE.CNT 15

RE

- (1) Bocan; ARTERIOSCLER, THROMB, VASC BIOL 2000, V20(1), P70 HCAPLUS
  - (2) Bocan; ATHEROSCLEROSIS 1998, V139(1), P21 HCAPLUS
  - (5) Bocan, T; WO 0004892 A 2000 HCAPLUS
  - (6) Bocan, T; ARTERIOSCLEROSIS AND THROMBOSIS 1991, V11, P1830 HCAPLUS
  - (7) Erba Carlo Spa; GB 2280675 A 1995 HCAPLUS
- ALL CITATIONS AVAILABLE IN THE RE FORMAT

L83 ANSWER 2 OF 13 HCAPLUS COPYRIGHT 2001 ACS

AN 2000:190909 HCAPLUS  
 DN 132:231975  
 TI Tryptophanyl esters and their N-acyl derivatives for the prevention and treatment of diseases caused or exacerbated by oxidative processes  
 IN Behl, Christian; Moosmann, Bernd  
 PA Max-Planck-Gesellschaft zur Foerderung der Wissenschaften e.V., Germany  
 SO PCT Int. Appl., 24 pp.  
 CODEN: PIXXD2  
 DT Patent  
 LA German  
 FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2000015206	A2	20000323	WO 1999-EP6819	19990915
	WO 2000015206	A3	20000810		
	W: JP, US				
	RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
	DE 19842416	A1	20000413	DE 1998-19842416	19980916
PRAI	DE 1998-19842416	A	19980916		

AB Tryptophanyl esters or their N-acyl derivs. are useful for prophylaxis and treatment of oxidative pathol. processes in degenerative diseases and/or carcinomas. Preferred compds. are tryptophan octyl ester, N-oleoyltryptophan Et ester, and N-dodecanoyltryptophan Et ester. The compds. are used for treatment and/or prophylaxis of neurodegenerative diseases, cataracts, neoplastic diseases, and/or cardiovascular diseases, esp. for Alzheimer's disease, Parkinson's disease, stroke, amyotrophic lateral sclerosis, cancer, arteriosclerosis, and/or myocardial infarction. Thus, tryptophan octyl ester (.gtoreq.4 nM) protected human neuroblastoma cells in vitro from oxidative stress damage (160 .mu.M H2O2).

IT **261734-92-3 261734-93-4**  
 RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (tryptophanyl esters and their N-acyl derivs. for prevention and treatment of diseases caused or exacerbated by oxidative processes)

L83 ANSWER 3 OF 13 HCAPLUS COPYRIGHT 2001 ACS  
 AN 1998:214200 HCAPLUS  
 DN 129:402  
 TI Effects of F-1394, an **acyl-CoA:cholesterol acyltransferase (ACAT)** inhibitor, on **ACAT** activity in HepG2 cells and on hepatic secretion of lipids in triton WR-1339-induced hyperlipidemic rats: possible role of hepatic **ACAT** in very low density lipoprotein secretion

AU Aragane, Katsumi; Kusunoki, Jun; Kitamine, Tetsuya; Yamaura, Tetsuaki; Ohnishi, Haruo  
 CS Pharmaceuticals Research Laboratories, Fujirebio, Inc., Tokyo, 192, Japan  
 SO Jpn. J. Pharmacol. (1998), 76(3), 309-312  
 CODEN: JJPAAZ; ISSN: 0021-5198  
 PB Japanese Pharmacological Society  
 DT Journal  
 LA English  
 AB We examd. the inhibitory potency of F-1394 ((1S,2S)-2-[3-(2,2-dimethylpropyl)-3-nonylureido]cyclohexane-1-yl 3-[4R-N-(2,2,5,5-tetramethyl-1,3-dioxane-4-carbonyl)amino]propionate), an **acyl-CoA:cholesterol acyltransferase (ACAT)** inhibitor, on **ACAT** activity and its hypolipidemic effect. F-1394 inhibited whole-cell **ACAT** activity in HepG2 cells with an IC50 value of 42 nM. The potency of F-1394 was greater than that of the five other **ACAT** inhibitors tested (YM-17E, CI-976, 57-118, CL-277082 and DL-melinamide). In rats made hyperlipidemic by Triton WR-1339, F-1394 caused a redn. in the hepatic secretion rate of **cholesterol**. These data suggest that inhibition of hepatic **ACAT** activity helps to reduce very low d. lipoprotein secretion from the liver into the circulation.

IT **9027-63-8, Cholesterol acyltransferase**

RL: BPR (Biological process); BIOL (Biological study); PROC (Process)  
(F-1394 inhibition of hepatic **cholesterol acyltransferase** leading to redn. of very low d. lipoproteins in hypolipidemic mechanism).

IT 71806-22-9

RL: BAC (Biological activity or effector, except adverse); BIOL (Biological study)  
(comparison with; F-1394 inhibition of hepatic **cholesterol acyltransferase** leading to redn. of very low d. lipoproteins in hypolipidemic mechanism)

L83 ANSWER 4 OF 13 HCAPLUS COPYRIGHT 2001 ACS

AN 1997:262611 HCAPLUS

DN 126:297659

TI Use of non-absorbable synthetic **sulfated polysaccharides** to decrease **cholesterol** absorption

IN Lange, Louis G. , III; Spilburg, Curtis A.

PA Lange, Louis G. , III, USA; Spilburg; Curtis A.

SO U.S., 20 pp. Cont. of U.S. Ser. No. 773,875, abandoned.

CODEN: USXXAM

DT Patent

LA English

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 5616570	A	19970401	US 1994-283723	19940801 <--
PRAI	US 1991-773875		19911018	<--	

AB This invention encompasses a method and compns. which inhibit pancreatic **cholesterol esterase** and triglyceride lipase and hence, lower **cholesterol** and triglycerides in the blood stream. **Sulfated pectin** was tested for **cholesterol esterase** inhibition and it had an IC50 of 0.6 mg/mL or 3.0 nM (assuming a mol. wt. of 200 kDa); importantly, native, **unsulfated pectin** did not inhibit **cholesterol esterase**, demonstrating the importance of **sulfation** for effective inhibition.

IT 75330-75-5, Lovastatin

RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(as addnl. agent; nonabsorbable synthetic **sulfated polysaccharides** to decrease **cholesterol** absorption)

IT 9026-00-0, **Cholesterol esterase**  
9027-63-8, **Cholesterol acyl transferase**

RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(inhibitors; nonabsorbable synthetic **sulfated polysaccharides** to decrease **cholesterol** absorption)

IT 1398-62-5, Chitin sulfate 9012-77-5  
9032-43-3, Cellulose sulfate 9042-14-2  
, Dextran sulfate 9047-13-6,  
Amylopectin sulfate 9049-31-4, Alginic acid sulfate 37293-26-8, Chitosan sulfate 65589-58-4

RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(nonabsorbable synthetic **sulfated polysaccharides** to decrease **cholesterol** absorption)

IT 9005-38-3, Sodium alginate

RL: RCT (Reactant)  
(prepn. of **sulfated alginate**; nonabsorbable synthetic **sulfated polysaccharides** to decrease **cholesterol** absorption)

L83 ANSWER 5 OF 13 HCAPLUS COPYRIGHT 2001 ACS

AN 1996:452005 HCAPLUS

DN 125:96066

TI Non-absorbable synthetic **sulfated** polysaccharides  
 IN **Lange, Louis G., III; Spilburg, Curtis A.;**  
**Reardan, Dayton T.**  
 PA Cv Therapeutics, Inc., USA  
 SO Eur. Pat. Appl., 25 pp.  
 CODEN: EPXXDW  
 DT Patent  
 LA English  
 FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	EP 712864	A2	19960522	EP 1995-307295	19951013 <--
	EP 712864	A3	19961016		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
	US 5521303	A	19960528	US 1994-322782	19941013 <--
	CA 2160440	AA	19960414	CA 1995-2160440	19951012 <--
	CA 2160440	C	19980825		
	AU 9534240	A1	19960426	AU 1995-34240	19951012 <--
	AU 682792	B2	19971016		
	JP 08253502	A2	19961001	JP 1995-265885	19951013 <--
PRAI	US 1994-322782		19941013 <--		
	US 1995-451563		19950526		
AB	This invention encompasses methods for manufg. purified, high mol. wt. <b>sulfated</b> polysaccharide compns. that inhibit pancreatic <b>cholesterol esterase</b> and lower cholesterol in the blood stream.				
IT	<b>9026-00-0, Cholesterol esterase</b> RL: BSU (Biological study, unclassified); BIOL (Biological study) (inhibitors; nonabsorbable synthetic <b>sulfated</b> polysaccharides for lowering blood cholesterol)				
IT	<b>57-88-5, Cholesterol, biological studies</b> RL: ADV (Adverse effect, including toxicity); BPR (Biological process); BIOL (Biological study); PROC (Process) (nonabsorbable synthetic <b>sulfated</b> polysaccharides for lowering blood cholesterol)				
IT	<b>9032-43-3P, Cellulose sulfate</b> RL: IMF (Industrial manufacture); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses) (nonabsorbable synthetic <b>sulfated</b> polysaccharides for lowering blood cholesterol)				
IT	<b>9004-34-6, Cellulose, reactions</b> RL: PEP (Physical, engineering or chemical process); RCT (Reactant); PROC (Process) (nonabsorbable synthetic <b>sulfated</b> polysaccharides for lowering blood cholesterol)				

L83 ANSWER 6 OF 13 HCAPLUS COPYRIGHT 2001 ACS

AN 1995:735432 HCAPLUS

DN 123:102789

TI Methods and reagents for inhibiting cholesterol absorption in humans mediated by pancreatic **cholesterol esterase**

IN **Lange, Louis G., III; Bosner, Matthew S.**

PA CV Therapeutics, Inc., USA

SO Can. Pat. Appl., 15 pp.

CODEN: CPXXEB

DT Patent

LA English

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	CA 2127230	AA	19950102	CA 1994-2127230	19940630 <--
	AU 9466101	A1	19950112	AU 1994-66101	19940630 <--
	EP 640620	A2	19950301	EP 1994-304793	19940630 <--
	EP 640620	A3	19951129		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE				
	JP 07165794	A2	19950627	JP 1994-151284	19940701 <--

PRAI US 1993-86517 19930701 <--

AB This invention relates to the human enzyme, pancreatic **cholesterol esterase** (PCE), and a receptor (PCER) for this protein expressed by cells of the intestinal lining. Specifically, the invention relates to the use of inhibitors of binding between PCE and PCER to reduce intestinal uptake of dietary cholesterol in humans. Antibodies, including antisera, and monoclonal and chimeric antibodies, and cell lines producing such antibodies, raised against the PCER protein or fragments or epitopes thereof, are also claimed. The invention also relates to the treatment of individuals with therapeutic drugs for the prevention or alleviation of disease states related to cholesterol metab.

IT **9026-00-0, Cholesterol esterase**

RL: BPR (Biological process); BIOL (Biological study); PROC (Process)  
(cholesterol-related diseases treatment with an inhibitor of pancreatic **cholesterol esterase** binding to its receptor)

L83 ANSWER 7 OF 13 HCAPLUS COPYRIGHT 2001 ACS

AN 1991:157212 HCAPLUS

DN 114:157212

TI The use of nonabsorbable synthetic **sulfated** polysaccharides to decrease cholesterol absorption

IN **Lange, Louis George, III; Spilburg, Curtis A.**

PA USA

SO PCT Int. Appl., 50 pp.

CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9012579	A1	19901101	WO 1990-US2079	19900420 <--
	W: AU, CA, JP, US, US				
	RW: AT, BE, CH, DE, DK, ES, FR, GB, IT, LU, NL, SE				
	US 5017565	A	19910521	US 1989-340868	19890420 <--
	US 5063210	A	19911105	US 1989-429398	19891031 <--
	CA 2053258	AA	19901021	CA 1990-2053258	19900420 <--
	CA 2053258	C	19980210		
	AU 9055356	A1	19901116	AU 1990-55356	19900420 <--
	AU 633569	B2	19930204		
	EP 469079	A1	19920205	EP 1990-907923	19900420 <--
	EP 469079	B1	19941207		
	R: AT, BE, CH, DE, DK, ES, FR, GB, IT, LI, LU, NL, SE				
	JP 04503813	T2	19920709	JP 1990-506819	19900420 <--
	JP 08019001	B4	19960228		
	ES 2064736	T3	19950201	ES 1990-907923	19900420 <--
	US 5484777	A	19960116	US 1993-167725	19931215 <--
PRAI	US 1989-340868		19890420	<--	
	US 1989-429398		19891031	<--	
	WO 1990-US2079		19900420	<--	
	US 1991-718280		19910620	<--	
	US 1992-928510		19920811	<--	

AB A method and compns. for inhibiting pancreatic **cholesterol esterase** and triglyceride lipase are disclosed. These compns. decrease cholesterol and triglyceride levels in blood. Oral administration of nonabsorbable inhibitors of **cholesterol esterase** inhibit the intestinal absorption of cholesterol. The anticholesteremics are **sulfated** alginic acid, pectin, amylopectin, chitin, dextran, cellulose, agar, and chitosan.

IT **57-88-5, Cholesterol, biological studies**

RL: BIOL (Biological study)  
(absorption of, by intestine, **sulfated** polysaccharide inhibition of)

IT **57-88-5**

RL: BIOL (Biological study)  
(anticholesteremics and Hypolipemics, **cholesterol esterase** inhibiting **sulfated** polysaccharides as)

- IT 1398-61-4D, Chitin, sulfated 9000-69-5D,  
Pectin, sulfated 9002-18-0D, Agar, sulfated  
9004-34-6D, Cellulose, sulfated, biological studies  
9004-54-0D, Dextran, sulfated, biological studies  
9005-32-7D, Alginic acid, sulfated 9012-76-4D,  
Chitosan, sulfated 9037-22-3D, Amylopectin,  
sulfated  
RL: BIOL (Biological study)  
(cholesterol absorption inhibition by)
- IT 9027-63-8  
RL: BIOL (Biological study)  
(inhibitors of, sulfated polysaccharides and, in treatment of  
hypercholesteremia)
- IT 9026-00-0, Cholesterol esterase  
RL: BIOL (Biological study)  
(inhibitors of, sulfated polysaccharides as, in treatment of  
hypercholesteremia)

L83 ANSWER 8 OF 13 HCAPLUS COPYRIGHT 2001 ACS

AN 1990:112089 HCAPLUS

DN 112:112089

TI Inhibition of intestinal cholesterol and fatty acid absorption with  
heparin or related substances

IN Lange, Louis G., III; Spilburg, Curtis A.; Kinnunen,  
Paula M.

PA Jewish Hospital of St. Louis, USA

SO PCT Int. Appl., 37 pp.

CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 8908456	A1	19890921	WO 1989-US787	19890227 <--
	W: AU, JP				
	RW: AT, BE, CH, DE, FR, GB, IT, LU, NL, SE				
	AU 8934348	A1	19891005	AU 1989-34348	19890227 <--
	US 5352601	A	19941004	US 1992-936103	19920826 <--
	US 5429937	A	19950704	US 1994-311862	19940926 <--
	US 5492822	A	19960220	US 1995-386433	19950210 <--
PRAI	US 1988-168424		19880315 <--		
	US 1989-312255		19890222 <--		
	WO 1989-US787		19890227 <--		
	US 1990-544212		19900626 <--		
	US 1991-655289		19910214 <--		
	US 1992-936103		19920826 <--		
	US 1994-311862		19940926 <--		

AB A method for inhibiting intestinal cell endogenous heparin-mediated  
absorption of cholesterol or fatty acids in mammals comprises orally  
administering to a mammal an effective amt. (5 mg-1g/day) of heparin, an  
active heparin subfraction, or heparinase. The fatty acids are those  
derived from the hydrolysis of cholesterol esters or triglycerides. Thus,  
male New Zealand white rabbits (1 kg) were fed 2% cholesterol Purina  
Rabbit Chow for two weeks plus either tap water or oral heparin (2 mg/mL)  
for 48 h prior to the expt. On day 15, the heparin-pretreated rabbits  
received 100 mg heparin in 10 mL water followed by 10 mL of radiolabeled  
liq. rabbit Chow contg. 50 .mu.Ci of [1,2,6,7-3H]cholesteryl oleate and  
the control group received 10 mL H2O followed by 10 mL of the same  
radiolabeled Chow. Compared to the control group, the heparin-treated  
group had 30% less 3H-cholesterol/cholesterol esters per mL of blood and  
50% less per g of liver.

IT 57-88-5, Cholesterol, biological studies

RL: BIOL (Biological study)

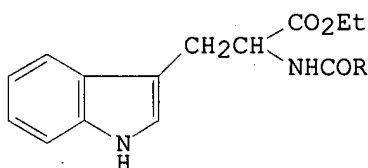
(absorption of, endogenous heparin-mediated, by intestine, inhibition  
of, with heparin or heparinase)

IT 9005-49-6, Heparin, biological studies



RL: BIOL (Biological study)  
 (cholesterol and fatty acid absorption by intestine inhibition with)  
 IT **57-88-5D, Cholesterol, esters**  
 RL: BIOL (Biological study)  
 (fatty acids from, absorption of, by intestine, heparin or heparinase inhibition of)  
 IT **9026-00-0, Cholesterol esterase**  
 RL: PRP (Properties)  
 (interaction of, with heparin, in heparin or heparinase inhibition of endogenous heparin-mediated cholesterol absorption by intestine)

L83 ANSWER 9 OF 13 HCAPLUS COPYRIGHT 2001 ACS  
 AN 1985:89686 HCAPLUS  
 DN 102:89686  
 TI Relative absorption of tryptophan ethyl ester amide derivatives with various fatty acid chains in the dog  
 AU Tse, Francis L. S.; Christiano, Juliet R.; Talbot, Kenrick C.  
 CS Drug Metab. Sect., Sandoz, Inc., East Hanover, NJ, 07936, USA  
 SO J. Pharm. Pharmacol. (1984), 36(9), 633-6  
 CODEN: JPPMAB; ISSN: 0022-3573  
 DT Journal  
 LA English  
 GI



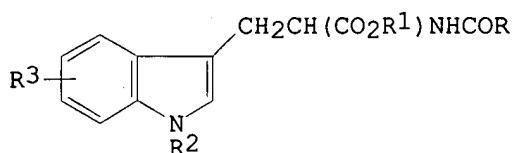
AB Sandoz compd. 57-118 is a mixt. of tryptophan Et ester amides (I, R = oleic, elaidic, linoleic, stearic, or palmitic acid moiety). The relative absorption of each of the 5 analogs was investigated in the dog following single oral doses of the homologous mixt. contg. 1 <sup>14</sup>C-labeled analog. It was shown that the extent of absorption of I (R = oleic acid) and its trans-isomer I (R = elaidic acid) were similar. An addnl. double bond in the fatty acid moiety (I, R = linoleic acid) facilitated gastrointestinal absorption. On the other hand, satd. fatty acid chains appeared to render the mols. less efficiently absorbed; the extent of absorption being dependent on the chain length. Thus, I (R = palmitic acid) with 16 carbon atoms on the fatty acid chain was better absorbed than I (R = stearic acid).

IT **71806-22-9 94921-32-1**  
 RL: BIOL (Biological study)  
 (absorption of, by intestine, fatty acid chain length and satn. in relation to)

L83 ANSWER 10 OF 13 HCAPLUS COPYRIGHT 2001 ACS  
 AN 1984:552341 HCAPLUS  
 DN 101:152341  
 TI N-Unsaturated fatty acid amides of tryptophan ester homologs and **anticholesteric** use thereof  
 IN Kathawala, Faizulla G.; Heider, John G.  
 PA Sandoz, Inc., USA  
 SO U.S., 9 pp. Cont.-in-part of U.S. Ser. No. 5,355, abandoned.  
 CODEN: USXXAM  
 DT Patent  
 LA English  
 FAN.CNT 4

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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PI	US 4448785	A	19840515	US 1982-391548	19820624 <--
	BE 873365	A1	19790709	BE 1979-9228	19790109 <--
	ZA 7900087	A	19800827	ZA 1979-87	19790109 <--
PRAI	US 1978-867813		19780109 <--		
	US 1979-5355		19790122 <--		
	US 1978-867824		19780109 <--		
	US 1978-872836		19780127 <--		
	US 1978-881780		19780227 <--		
	US 1978-881781		19780227 <--		
	US 1978-891298		19780329 <--		
	BE 1979-1009228		19790109 <--		
GI					



I

AB **Anticholesteremic** tryptophans I (RCO = unsatd. long-chain fatty acyl; R1 = alkyl, benzyl; R2 = H, alkyl, benzyl; R3 = H, halo, alkyl, alkoxy) were prepd. by N-acylation of tryptophan esters. Thus, linoleic acid was treated with ClCO2Et in CH2Cl2 contg. Et3N and the resulting mixed anhydride condensed with DL-Trp-OEt.HCl to give I (RCO = linoleoyl, R1 = Et, R2 = R3 = H) (II). At 10 mg/mL II inhibited 59-69% the accumulation of **cholesterol** ester in Fu5AH cells.

IT **71806-22-9P**

RL: SPN (Synthetic preparation); PREP (Preparation)  
(prepn. of)

L83 ANSWER 11 OF 13 HCAPLUS COPYRIGHT 2001 ACS

AN 1984:45116 HCAPLUS

DN 100:45116

TI Role of **acyl CoA:cholesterol**

**acyltransferase** in **cholesterol** absorption and its inhibition by 57-118 in the rabbit

AU **Heider, John G.**; Pickens, Carolyn E.; Kelly, Lawrence A.

CS Sandoz, East Hanover, NJ, 07936, USA

SO J. Lipid Res. (1983), 24(9), 1127-34

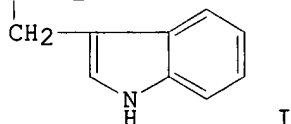
CODEN: JLPRAW; ISSN: 0022-2275

DT Journal

LA English

GI

Me(CH2)7CH=CH(CH2)7CONHCHCO2Et



I

AB Esterification of **cholesterol** in rabbit small intestine mucosal microsomes by **acyl CoA:cholesterol** **acyltransferase** (EC 2.3.1.26) (ACAT) [9027-63-8] and mucosal cytosol by **cholesterol esterase** (EC 3.1.1.13) was studied. Compd. 57-118 [N-(1-oxo-9-octadecenyl)-DL-tryptophan(Z)ethyl ester] (I) [71806-22-9] an inhibitor of **cholesterol** absorption, inhibited in vitro ACAT in

mucosal microsomes at concns. of 2-20 nmol/0.5 mL incubation mixt., but had no effect on **cholesterol esterase** in the cytosol at similar concns. A kinetic anal. using a Lineweaver-Burk plot indicates that I acts as a competitive inhibitor of **ACAT**. An ex vivo study in the rabbit where I was given by gavage at a dose of 200 mg/kg also showed inhibition of **ACAT** but not of **cholesterol esterase**. High-performance liq. chromatog. detn. of I in various subcellular fractions demonstrated the presence of this substance after oral administration in concns. in mucosal microsomes equiv. to those required to show inhibition of **ACAT** in vitro. These data support the work of K. R. Norum et al. (1979) indicating that mucosal **ACAT** plays a significant role in **cholesterol** absorption.

IT 57-88-5, biological studies

RL: BIOL (Biological study)

(absorption of, by intestine, compd. 57-118 effect on, **cholesterol acyltransferase** in relation to)

IT 71806-22-9

RL: BIOL (Biological study)

(**cholesterol acyltransferase** of small intestine mucosa inhibition by)

IT 9027-63-8

RL: PROC (Process)

(of small intestine mucosa, compd. 57-118 inhibition of)

L83 ANSWER 12 OF 13 HCAPLUS COPYRIGHT 2001 ACS

AN 1981:174880 HCAPLUS

DN 94:174880

TI Pharmaceutical long-chain fatty acid amides of tryptophan derivatives

IN Heider, John G.; Kathawala, Faizulla Gulamhusein

PA Sandoz-Patent-G.m.b.H., Fed. Rep. Ger.

SO Ger. Offen., 20 pp.

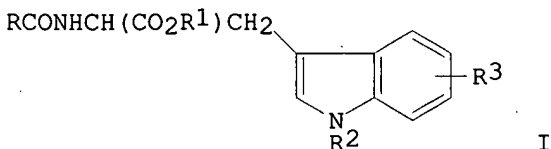
CODEN: GWXXBX

DT Patent

LA German

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE	
PI	DE 3024739	A1	19810129	DE 1980-3024739	19800630	<--
	GB 2052985	A	19810204	GB 1980-22202	19800707	<--
	JP 56032457	A2	19810401	JP 1980-91828	19800707	<--
	FR 2460931	A1	19810130	FR 1980-15237	19800709	<--
	FR 2460931	B1	19830624			
PRAI	US 1979-55801		19790709			<--
GI						



AB The **anticholesteremic** (no data) compds. I (R = C<sub>7</sub>-23 aliph. group contg. 1-4 double bonds or .alpha.,.beta.-methylene bridges; R<sup>1</sup> = H, cation; R<sup>2</sup> = H, Cl-8 alkyl, PhCH<sub>2</sub>; R<sup>3</sup> = H, F, Cl, Br, Cl-3 alkyl or alkoxy) were prep'd. Thus, I (RCO = oleyl, R<sup>1</sup>-R<sup>3</sup> = H) was obtained by sapon. of the corresponding I (R<sup>1</sup> = Et).

IT 71806-22-9

RL: RCT (Reactant)

(sapon. of)

L83 ANSWER 13 OF 13 HCAPLUS COPYRIGHT 2001 ACS

AN 1979:593639 HCAPLUS

DN 91:193639  
 TI Fatty acid amide and hydrazide derivatives  
 IN Kathawala, Faizulla Gulamhusein; Heider, John G.  
 PA Sandoz-Patent-G.m.b.H., Switz.  
 SO Ger. Offen., 37 pp.

CODEN: GWXXBX

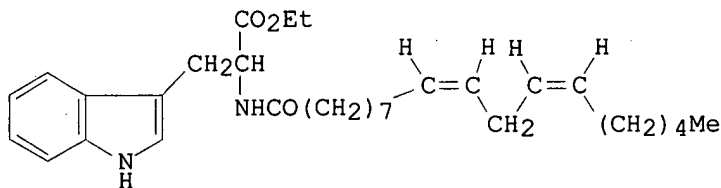
DT Patent

LA German

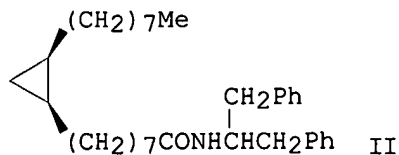
FAN.CNT 4

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	DE 2856856	A1	19790712	DE 1978-2856856	19781230 <--
	US 4229463	A	19801021	US 1978-881780	19780227 <--
	US 4194002	A	19800318	US 1978-891298	19780329 <--
	CH 644842	A	19840831	CH 1979-3	19790102 <--
	DK 7900030	A	19790710	DK 1979-30	19790103 <--
	FI 7900025	A	19790710	FI 1979-25	19790104 <--
	NL 7900084	A	19790711	NL 1979-84	19790105 <--
	GB 2012261	B2	19821222	GB 1979-337	19790105 <--
	GB 2012261	A	19790725		
	SE 7900142	A	19790710	SE 1979-142	19790108 <--
	SE 446093	B	19860811		
	SE 446093	C	19861120		
	JP 54109930	A2	19790829	JP 1979-138	19790108 <--
	JP 63023987	B4	19880518		
	ES 476648	A1	19791216	ES 1979-476648	19790108 <--
	CA 1101871	A1	19810526	CA 1979-319259	19790108 <--
	IL 56393	A1	19820831	IL 1979-56393	19790108 <--
	AT 7900118	A	19840615	AT 1979-118	19790108 <--
	AT 376962	B	19850125		
	BE 873365	A1	19790709	BE 1979-9228	19790109 <--
	AU 7943233	A1	19790719	AU 1979-43233	19790109 <--
	AU 529328	B2	19830602		
	FR 2416885	A1	19790907	FR 1979-438	19790109 <--
	FR 2416885	B1	19830422		
	ZA 7900087	A	19800827	ZA 1979-87	19790109 <--
	US 4185118	A	19800122	US 1979-2974	19790112 <--
	US 4248893	A	19810203	US 1979-9473	19790205 <--
	US 4201785	A	19800506	US 1979-27019	19790404 <--
PRAI	US 1978-867813		19780109		<--
	US 1978-867824		19780109		<--
	US 1978-872836		19780127		<--
	US 1978-881780		19780227		<--
	US 1978-881781		19780227		<--
	US 1978-891298		19780329		<--
	DE 1978-2856856		19781230		<--
	BE 1979-1009228		19790109		<--

GI



I



II

AB A wide range of title compds. (e.g., I, II) bearing unsatd. aliph. groups on the N atom(s) were prepd. as agents for combating arteriosclerosis by controlling blood **cholesterol** levels. Thus, linoleic acid, ClCO<sub>2</sub>Et, and (.-.-)-tryptophan Et ester-HCl gave I.

IT **71806-22-9P**  
RL: SPN (Synthetic preparation); PREP (Preparation)  
(prepn. of)

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L148 ANSWER 1 OF 11 EMBASE COPYRIGHT 2001 ELSEVIER SCI. B.V.

AN 94038358 EMBASE

DN 1994038358

TI Inhibition of inducible nitric oxide synthase in macrophages by oxidized low-density lipoproteins.

AU Yang X.; Cai B.; Sciacca R.R.; Cannon P.J.

CS Columbia University, 630 W 168th St, New York, NY 10032, United States

SO Circulation Research, (1994) 74/2 (318-328).

ISSN: 0009-7330 CODEN: CIRUAL

CY United States

DT Journal; Article

FS 018 Cardiovascular Diseases and Cardiovascular Surgery

029 Clinical Biochemistry

LA English

SL English

AB Uptake of oxidized low-density lipoprotein (LDL) by monocyte/macrophages to form 'foam' cells has been implicated in atherogenesis. Activated monocyte/macrophages synthesize nitric oxide (NO) from L-arginine. NO is cytotoxic, antiproliferative, and a vasodilator that inhibits platelet and monocyte adhesion. NO synthase mRNA, protein, and enzyme activity were induced in J774.A1 macrophages activated with **lipopolysaccharide** and gamma interferon. When macrophages were incubated with oxidized LDL for 24 hours and activated, there was a dose- and time-dependent inhibition of NO synthesis, assessed as nitrite accumulation in the media. When activated cells were incubated with nontoxic doses of lipoprotein (25 .mu.g/mL), neither native LDL nor acetyl LDL inhibited NO production, whereas oxidized LDL produced 50% inhibition. Levels of enzyme protein were unchanged by Western blot. Inhibition was a function of the degree of oxidation of LDL but was independent of **cholesteryl** esterification by the cells. Incubations of oxidized LDL with cells that had been pretreated with **dextran sulfate** or cytochalasin B yielded no evidence that inhibition was dependent on the scavenger receptor or directed endocytosis. Kinetic studies of inducible NO synthase from J774.A1 cells that were incubated with increasing doses of oxidized LDL indicated a pattern of noncompetitive inhibition. Inhibition of the enzyme was produced by lipids extracted from oxidized LDL but not by lipids extracted from native LDL. Because phosphatidylcholine (PC) is converted to lysophosphatidylcholine (LPC) during the oxidation of LDL, the effects of LPC were investigated. PC vesicles containing LPC did not inhibit enzyme activity but produced modest reductions in nitrite accumulation from cells. In contrast, PC vesicles had no significant effect. The data indicate that oxidized LDL lipid inhibits the activity of inducible NO synthase in activated macrophages. NO production by this enzyme and its inhibition by oxidized

LDL lipid may influence cell-to-cell interactions and vasomotor tone in atherosclerotic blood vessels.

CT Medical Descriptors:

\*atherosclerosis

animal cell

article

cell stimulation

controlled study

enzyme activity

enzyme inhibition

lipid oxidation

macrophage activation

mouse

nonhuman

priority journal

Drug Descriptors:

\*low density lipoprotein

\*nitric oxide synthase

RN (nitric oxide synthase) 125978-95-2

L148 ANSWER 2 OF 11 EMBASE COPYRIGHT 2001 ELSEVIER SCI. B.V.

AN 92122604 EMBASE

DN 1992122604

TI Nutrition and therapeutics.

AU Nestel P.J.; Eisenberg S.

CS Australia

SO Current Opinion in Lipidology, (1992) 3/1 (1-4).

ISSN: 0957-9672 CODEN: COPLEU

CY United Kingdom

DT Journal; Editorial

FS 017 Public Health, Social Medicine and Epidemiology

018 Cardiovascular Diseases and Cardiovascular Surgery

029 Clinical Biochemistry

037 Drug Literature Index

038 Adverse Reactions Titles

LA English

CT Medical Descriptors:

\*lipoprotein metabolism

\*nutrition

apheresis

atherosclerosis

bile acid metabolism

blood viscosity

cholesterol blood level

cholesterol metabolism

drug tolerance

drug use

editorial

erythrocyte aggregation

food composition

heart disease: PC, prevention

heart infarction prevention

human

human cell

hypercholesterolemia: TH, therapy

hyperlipidemia: DT, drug therapy

immunoabsorption

major clinical study

oxidation

patient selection

protein polymorphism

public health

side effect

treatment planning

Drug Descriptors:

acipimox: PD, pharmacology

antioxidant

**apolipoprotein: EC, endogenous compound**

**apolipoprotein e: EC, endogenous compound**

beta carotene

bezafibrate

bile acid: EC, endogenous compound

**cholesterol: EC, endogenous compound**

**cholesterol acyltransferase: EC, endogenous compound**

**dextran sulfate**

enzyme inhibitor: DV, drug development

fenofibrate

fibric acid derivative: PD, pharmacology

fibric acid derivative: AE, adverse drug reaction

fibrinogen: EC, endogenous compound

fish oil

gemfibrozil

heparin

**high density lipoprotein cholesterol: EC, endogenous compound**

**hydroxymethylglutaryl coenzyme a reductase inhibitor: CB, drug**

**combination**

hydroxymethylglutaryl coenzyme a reductase inhibitor: AE, adverse drug reaction

hydroxymethylglutaryl coenzyme a reductase inhibitor: PD, pharmacology

linoleic acid

**low density lipoprotein cholesterol: EC, endogenous compound**

**mevinolin**

nicotinic acid: DT, drug therapy

nicotinic acid: DV, drug development

polyunsaturated fatty acid

pravastatin

probucol: DT, drug therapy

probucol: DV, drug development

simvastatin

RN (acipimox) 51037-30-0; (beta carotene) 7235-40-7; (bezafibrate)

41859-67-0; (**cholesterol**) 57-88-5; (

**cholesterol acyltransferase**) 9027-63-8; (

**dextran sulfate**) 9011-18-1, 9042-14-2;

(fenofibrate) 49562-28-9; (fibrinogen) 9001-32-5; (fish oil) 8016-13-5;

(gemfibrozil) 25812-30-0; (heparin) 37187-54-5, 8057-48-5, 8065-01-8,

9005-48-5; (linoleic acid) 1509-85-9, 2197-37-7, 60-33-3, 822-17-3; (

**mevinolin**) 75330-75-5; (nicotinic acid) 54-86-4,

59-67-6; (pravastatin) 81131-74-0; (probucol) 23288-49-5; (simvastatin)

79902-63-9

L148 ANSWER 3 OF 11 EMBASE COPYRIGHT 2001 ELSEVIER SCI. B.V.

AN 89050064 EMBASE

DN 1989050064

TI Regulation of 12-hydroxyeicosatetraenoic acid synthesis by acetyl-LDL in mouse peritoneal macrophages.

AU Mathur S.N.; Albright E.; Field F.J.

CS Department of Internal Medicine, University of Iowa, Iowa City, IA 52242, United States

SO Biochimica et Biophysica Acta - Lipids and Lipid Metabolism, (1989) 1001/1 (50-59).

ISSN: 0005-2760 CODEN: BBLA6

CY Netherlands

DT Journal

FS 029 Clinical Biochemistry

LA English

SL English

AB The mechanism for the regulation of 12-hydroxyeicosatetraenoic acid (12-HETE) production by **cholesterol**-rich macrophages was investigated. .beta.-VLDL and acetyl-LDL, lipoproteins which result in **cholesterol** accumulation in macrophages, stimulated 12-HETE secretion. Lipoproteins which do not induce **cholesterol** accumulation, such as low- and high-density lipoproteins, did not.

Cell-free homogenates from **cholesterol**-rich macrophages had significantly more 12-lipoxygenase activity than homogenates from unmodified cells. Preincubating homogenates prepared from unmodified macrophages with acetyl-LDL, LDL or multilamellar liposomes containing total lipids from acetyl-LDL but not apoproteins significantly increased 12-lipoxygenase activity. This stimulatory effect was caused by the phospholipid moiety of the lipoprotein. 12-HETE synthesis was not increased in macrophages enriched 6-fold in unesterified **cholesterol**. Acetyl-LDL stimulated 12-HETE synthesis in macrophages in which **cholesteryl** ester accumulation was prevented by inhibiting acylcoenzyme A: **cholesterol acyltransferase** activity. When binding of acetyl-LDL to its receptor was decreased by increasing concentrations of **dextran sulfate**, or when lysosomal metabolism of the lipoprotein was prevented by chloroquine, 12-HETE production significantly decreased. Moreover, the **combination** of inhibiting acetyl-LDL binding and degradation completely blocked the stimulation of 12-HETE synthesis by acetyl-LDL. The data indicate that acetyl-LDL must enter the macrophage and be partially degraded to regulate 12-HETE synthesis. The regulation is independent of **cholesterol** accumulation but is related to the entering lipoprotein phospholipid.

CT Medical Descriptors:

\***cholesterol acetyltransferase**

mouse

animal cell

nonhuman

priority journal

Drug Descriptors:

\*12 hydroxyicosatetraenoic acid

\*arachidonate 12 lipoxygenase

\***cholesterol**

\***low density lipoprotein**

\*phospholipid

\***very low density lipoprotein**

radioisotope

RN (12 hydroxyicosatetraenoic acid) 54397-83-0, 59985-28-3, 71030-37-0;  
(arachidonate 12 lipoxygenase) 82391-43-3; (**cholesterol**)  
57-88-5

L148 ANSWER 4 OF 11 EMBASE COPYRIGHT 2001 ELSEVIER SCI. B.V.

AN 84089976 EMBASE

DN 1984089976

TI The interaction of human apoB-containing lipoproteins with mouse peritoneal macrophages: A comparison of Lp(a) with LDL.

AU Krempler F.; Kostner G.M.; Roscher A.; et al.

CS First Department of Medicine, Landeskrankenanstalten, A-5020 Salzburg, Austria

SO Journal of Lipid Research, (1984) 25/3 (283-287).

CODEN: JLPRAW

CY United States

DT Journal

FS 029 Clinical Biochemistry

018 Cardiovascular Diseases and Cardiovascular Surgery

023 Nuclear Medicine

LA English

AB **Cholesteryl** ester accumulation in macrophages and foam cell formation is believed to play an important role in atherogenesis. The effect of Lp(a) on the incorporation of [<sup>14</sup>C]oleate into **cholesteryl** esters was studied in mouse peritoneal macrophages. In view of the physico-chemical similarities between Lp(a) and LDL, the results were compared with those obtained with LDL. Native Lp(a) and LDL did not stimulate **cholesteryl** ester formation. Incubation of macrophages with Lp(a)- or LDL-dextran sulfate complexes caused a significant increase in **cholesteryl** ester formation. A similar effect was observed when Lp(a) or LDL were incubated with macrophages in the presence of antibodies directed against the



specific Lp(a) apoprotein or against LpB. Treatment of Lp(a) with acetic anhydride or malondialdehyde (MDA) was followed by precipitation of most of the lipoprotein. Therefore, these modifications were not suitable to study the uptake of modified Lp(a) by macrophages. Studies with acetyl-LDL or MDA-treated LDL caused the well-known stimulation of [<sup>14</sup>C]oleate incorporation into **cholesteryl** esters. Thus, the modification of Lp(a) by **sulfated polysaccharides** or by treatment with antibodies yields similar **cholesteryl** ester deposition in mouse peritoneal macrophages as observed with modified LDL. This might be one mechanism by which Lp(a) exerts its atherogenicity.

CT Medical Descriptors:  
 oleic acid c 14  
 peritoneum macrophage  
 etiology  
 animal cell  
 nonhuman  
 mouse  
 peritoneum  
 Drug Descriptors:  
 \*apolipoprotein b  
 \*lipoprotein  
 \*lipoprotein a  
 \*low density lipoprotein  
 cholesterol ester  
 radioisotope

L148 ANSWER 5 OF 11 EMBASE COPYRIGHT 2001 ELSEVIER SCI. B.V.

AN 83041541 EMBASE

DN 1983041541

TI Distribution of lecithin-**cholesterol acyltransferase** (LCAT) in human plasma lipoprotein fractions. Evidence for the association of active LCAT with low density lipoproteins.

AU Chen C.H.; Albers J.J.

CS Dep. Med., Harborview Med. Cent., Univ. Washington Sch. Med., Seattle, WA 98195, United States

SO Biochemical and Biophysical Research Communications, (1982) 107/3 (1091-1096).

CODEN: BBRCA

CY United States

DT Journal

FS 029 Clinical Biochemistry

LA English

AB The distribution of lecithin-**cholesterol acyltransferase** (LCAT) in human plasma was assessed by measuring both LCAT mass and activity in plasma fractions separated by **sequential** flotation ultracentrifugation, single-spin gradient ultracentrifugation, **dextran sulfate-Mg<sup>2+</sup>** precipitation or agarose gel filtration. Although most of the LCAT was found to be associated with the high density lipoprotein fraction, a small amount of active LCAT (approximately 1% of the plasma LCAT mass and activity) was consistently associated with the low density lipoprotein fraction. LCAT was not found in the very low density lipoprotein fraction. The LDL-associated LCAT may play an important role in the acylation of lysolecithin by lysolecithin acyltransferase activity of LCAT.

CT Medical Descriptors:  
 plasma  
 human cell  
 human  
 normal human  
 Drug Descriptors:  
 \*phosphatidylcholine sterol acyltransferase  
 \*lipoprotein  
 \*low density lipoprotein

RN (phosphatidylcholine sterol acyltransferase) 9031-14-5

L148 ANSWER 6 OF 11 EMBASE COPYRIGHT 2001 ELSEVIER SCI. B.V.

AN 82122285 EMBASE  
DN 1982122285  
TI Lymphocyte-conditioned medium protects human monocyte-macrophages from **cholesteryl** ester accumulation.  
AU Fogelman A.M.; Seager J.; Haberland M.E.; et al.  
CS Div. Cardiol., Dept. Med., Sch. Med., UCLA, Los Angeles, CA 90024, United States  
SO Proceedings of the National Academy of Sciences of the United States of America, (1982) 79/3 I (922-926).  
CODEN: PNASA6  
CY United States  
DT Journal  
FS 029 Clinical Biochemistry  
018 Cardiovascular Diseases and Cardiovascular Surgery  
LA English  
AB Exposure of human monocyte-macrophages to as little as 50 .mu.l of culture medium from lymphocytes stimulated by concanavalin A (Con A) resulted in a dramatic decrease in the activities of the low density lipoprotein (LDL) receptor pathway, the LDL-**dextran sulfate** pathway, and the scavenger receptor pathway. This effect was not seen when the monocyte-macrophages were exposed to culture medium from lymphocytes cultured without Con A or with Con A **together** with .alpha.-methyl mannoside or control medium without lymphocytes. The activity of 3-hydroxy-3-methylglutaryl-coenzyme A reductase also decreased in monocyte-macrophages exposed to culture medium from stimulated lymphocytes. **Acyl-CoA-cholesterol O-acyltransferase** activity, protein synthesis, protein content, phagocytosis of heat-killed yeast, and non-receptor-mediated endocytosis were not inhibited. Monocyte-macrophages exposed to malondialdehyde altered-LDL in the presence of stimulated lymphocyte culture medium accumulated substantially less **cholesteryl** esters than did cells in control medium. The authors propose that substances produced by stimulated lymphocytes may be useful in protecting macrophages from **cholesteryl** ester accumulation.  
CT Medical Descriptors:  
\*lymphocyte  
\*macrophage  
\*monocyte  
protein synthesis  
human cell  
normal human  
blood and hemopoietic system  
lymphatic system  
Drug Descriptors:  
\***cholesterol ester**  
**cholesterol acyltransferase**  
hydroxymethylglutaryl coenzyme a reductase  
**low density lipoprotein**  
RN (**cholesterol acyltransferase**) 9027-63-8;  
(hydroxymethylglutaryl coenzyme a reductase) 37250-24-1  
  
L148 ANSWER 7 OF 11 EMBASE COPYRIGHT 2001 ELSEVIER SCI. B.V.  
AN 82031845 EMBASE  
DN 1982031845  
TI **Cholesterol** synthesis and esterification in experimental xanthoma tissues.  
AU Kodama H.; Nagao Y.; Arakawa K.; et al.  
CS Dept. Dermatol., Okayama Univ. Med. Sch., Shikata, Okayama 700, Japan  
SO Journal of Lipid Research, (1981) 22/7 (1033-1041).  
CODEN: JLPRAW  
CY United States  
DT Journal  
FS 029 Clinical Biochemistry  
013 Dermatology and Venereology  
018 Cardiovascular Diseases and Cardiovascular Surgery  
LA English

AB We studied **cholesterol** metabolism in experimental xanthoma tissues which were induced by injection of high molecular weight sodium **dextran sulfate** into the dermis of **hypercholesterolemic** rabbits. Control studies were performed on dermal specimens of the **dextran sulfate**-injected site of normolipemic rabbits. **Cholesterol** accumulation was much greater in the **hypercholesterolemic** rabbit tissues than in the normolipemic rabbit tissues. Histiocytes and foam cells in such lesions had an ability to synthesize **cholesterol**. However, **cholesterol** synthesis was suppressed in the **cholesterol**-rich tissues of **hypercholesterolemic** rabbits. This suppression was obviously caused by the accumulation of **cholesterol** in the tissues which take up lipoprotein in **hypercholesterolemic** rabbits. On the other hand, esterification of **cholesterol** was greater in the **hypercholesterolemic** rabbit tissues than in the normolipemic rabbit tissues. **Cholesterol** was esterified more selectively with oleic acid than with palmitic acid. Therefore, **cholesteryl** oleate increased in the tissues **concomitantly** with the accumulation of **cholesteryl** esters. Fatty acids of serum origin rather than those synthesized in situ were more important in the esterification process. It was suggested that **cholesterol** esterification was mediated by acyl-coenzyme A:**cholesterol** **acyltransferase** and that lecithin:**cholesterol** **acyltransferase** contributed little to the process.

CT Medical Descriptors:

\***cholesterol** esterification

\***hypercholesterolemia**

\*xanthoma

in vitro study

animal experiment

Drug Descriptors:

\***cholesterol**

**cholesterol** **acyltransferase**

RN (**cholesterol**) 57-88-5; (**cholesterol** **acyltransferase**) 9027-63-8

L148 ANSWER 8 OF 11 EMBASE COPYRIGHT 2001 ELSEVIER SCI. B.V.

AN 82006160 EMBASE

DN 1982006160

TI Observations on the pathogenesis of xanthoma.

AU Kodama H.; Arakawa K.; Nagao Y.; et al.

CS Dept. Dermatol., Okayama Med. Sch., Okayama, Japan

SO Nishinohon Journal of Dermatology, (1981) 43/4 (566-570).

CODEN: NNHIAN

CY Japan

DT Journal

FS 013 Dermatology and Venereology

LA Japanese

SL English

AB Our observations on the pathogenesis of xanthoma were reported. Direct immunofluorescence using anti-human .beta.-lipoprotein antibody indicated that human .beta.-lipoprotein was incorporated into foam cells of human xanthomas and an experimental rabbit xanthoma which was induced by human .beta.-lipoprotein immune complexes in the blood stream. Foam cells originate from scavenger cells, such as dermal histiocytes and not from fibroblasts. Histiocytes incorporate more readily denatured lipoproteins than lipoproteins of native form. **Cholesterol** metabolism was investigated in experimental xanthoma tissues which were induced by intradermal **dextran sulfate** injection.

**Cholesterol** synthesis was suppressed and **cholesterol** esterification was increased in the **cholesterol**-rich xanthoma tissues. **Cholesterol** was esterified more selectively with oleic acid than with palmitic acid. Therefore, **cholesterol** oleate increases in the tissues **concomitantly** with the accumulation of **cholesteryl** esters. The more important role in the esterification was played by the fatty acids of serum origin rather than those

synthesized in situ. These findings suggest that the **cholesterol** esterification was mediated by **acyl-CoA: cholesterol acyltransferase** and that lecithin: **cholesterol acyltransferase** had contributed little to the esterification.

CT Medical Descriptors:

\*xanthoma  
theoretical study  
human cell  
etiology  
histology  
cytology

Drug Descriptors:

\*low density lipoprotein  
\*cholesterol

RN (cholesterol) 57-88-5

L148 ANSWER 9 OF 11 EMBASE COPYRIGHT 2001 ELSEVIER SCI. B.V.

AN 79110459 EMBASE

DN 1979110459

TI Binding site on macrophages that mediates uptake and degradation of acetylated low density lipoprotein, producing massive **cholesterol** deposition.

AU Goldstein J.L.; Ho Y.K.; Basu S.K.; Brown M.S.

CS Dept. Molec. Genet., Univ. Texas Hlth Sci. Cent., Dallas, Tex. 75235, United States

SO Proceedings of the National Academy of Sciences of the United States of America, (1979) 76/1 (333-337).

CODEN: PNASA6

CY United States

DT Journal

FS 029 Clinical Biochemistry

018 Cardiovascular Diseases and Cardiovascular Surgery

LA English

AB Resident mouse peritoneal macrophages were shown to take up and degrade acetylated 125I-labeled low density lipoprotein (125I-acetyl-LDL) in vitro at rates that were 20-fold greater than those for the uptake and degradation of 125I-LDL. The uptake of 125I-acetyl-LDL and its subsequent degradation in lysosomes were attributable to a high-affinity, trypsin-sensitive, surface binding site that recognized acetyl-LDL but not native LDL. When 125I-acetyl-LDL was bound to this site at 4.degree.C and the macrophages were subsequently warmed to 37.degree.C, 75% of the cell-bound radioactivity was degraded to mono[125I]iodotyrosine within 1 hr. The macrophage binding site also recognized maleylated LDL, maleylated albumin, and two **sulfated polysaccharides** (fucoidin and **dextran sulfate**) indicating that negative charges were important in the binding reaction. A similar binding site was present on rat peritoneal macrophages, guinea pig Kupffer cells, and cultured human monocytes but not on human lymphocytes or fibroblasts, mouse L cells or Y-1 adrenal cells, or Chinese hamster ovary cells. Uptake and degradation of acetyl-LDL via this binding site stimulated **cholesterol** esterification 100-fold and produced a 38-fold increase in the cellular content of **cholesterol** in mouse peritoneal macrophages. although the physiologic significance, if any, of this macrophage uptake mechanism is not yet known, we hypothesize that it may mediate the degradation of denatured LDL in the body and thus serve as a 'backup' mechanism for the previously described receptor-mediated degradation of native LDL that occurs in parenchymal cells. Such a scavenger pathway might account for the widespread deposition of LDL-derived **cholesteryl** esters in macrophages of patients with familial **hypercholesterolemia** in whom the parenchymal cell pathway for LDL degradation is blocked, owing to a genetic deficiency of receptors for native LDL.

CT Medical Descriptors:

in vitro study  
animal experiment

mouse  
peritoneum  
Drug Descriptors:  
  \***cholesterol**  
  \***low density lipoprotein**  
radioisotope

RN (cholesterol) 57-88-5

L148 ANSWER 10 OF 11 EMBASE COPYRIGHT 2001 ELSEVIER SCI. B.V.

AN 79095290 EMBASE

DN 1979095290

TI The influence of various lipoproteins and apolipoproteins on the in vitro esterification of **cholesterol** in human serum by the enzyme lecithin: **cholesterol acyltransferase**.

AU Kostner G.M.

CS Inst. Med. Biochem., Univ. Graz, Austria

SO Scandinavian Journal of Clinical and Laboratory Investigation, (1978) 38/SUPPL. 150 (66-71).

CODEN: SJCLAY

CY Norway

DT Journal

FS 029 Clinical Biochemistry

003 Endocrinology

LA English

AB The influence of various lipoproteins, apolipoproteins, and lipoprotein lipids on the initial rate of **cholesterol** esterification (IRE) by the enzyme lecithin:**cholesterol acyltransferase** (LCAT) has been studied in vitro in sera from normolipemic and hyperlipemic human subjects. This was achieved by adding isolated lipoprotein density fractions and families to fresh sera, on the one hand, and by specific adsorption of distinct lipoprotein classes with antibodies and polyanions on the other. The results were as follows: (1) Addition of all known lipoprotein density classes to normal serum, except for HDL2, had no influence on the IRE but reflected to some degree the mode of assay system. Addition of HDL2 inhibited the LCAT and the inhibitor was chloroform methanol extractable. The addition of LpC, a minor fraction from HDL of all normal sera, markedly enhanced the IRE. (2) Removal of VLDL plus LDL by antibodies or **dextran sulfate** had little if any effect. After precipitation of all LpA with anti-AI, approximately 50% of the LCAT activity remained in the supernatant and was active even in the assays where only endogenous substrate was provided. In the precipitated LpA the rest of the activity was found, despite the fact that antigenic determinants of apoAI were blocked by antibodies. The removal of LpC from the HDL-class was followed by a complete abolishment of LCAT activity. This activity, however, could partly be restored by adding exogenous substrate. (3) The IRE was found to be increased in persons with primary and post-prandial hypertriglyceridemia. In these cases the concentration of the LpC in HDL was also increased. These findings suggest that LpC of HDL plays a major role in the esterification of **cholesterol** in human serum under physiological conditions.

CT Medical Descriptors:

human cell

normal human

blood and hemopoietic system

Drug Descriptors:

\***apolipoprotein**

\*phosphatidylcholine sterol acyltransferase

\***lipoprotein**

RN (phosphatidylcholine sterol acyltransferase) 9031-14-5

L148 ANSWER 11 OF 11 EMBASE COPYRIGHT 2001 ELSEVIER SCI. B.V.

AN 78218564 EMBASE

DN 1978218564

TI [Determination of lecithin-**cholesterol acyltransferase** . Studies on the precipitation of .beta.-lipoproteins by **dextran sulphate**].

DOSAGE DE LA LECITHINE-**CHOLESTEROL** ACYLTRANSFERASE.  
INTERET DE LA PRECIPITATION DES .beta.-LIPOPROTEINES PAR LE SULFATE DE  
DEXTRANE.

AU Alcindor L.G.; Melin B.; Benhamou G.; Piot M.C.

CS Lab. Biochem., Fac. Med., Paris, France

SO Clinica Chimica Acta, (1977) 81/2 (177-182).

CODEN: CCATAR

CY Netherlands

DT Journal

FS 029 Clinical Biochemistry

LA English

AB Uncertainties in assays of lecithin-**cholesterol**

**acyltransferase** (LCAT) are generally related to the degree of isotopic equilibrium obtained by rapid exchange of unesterified **cholesterol** between the different lipoproteins. A new method is presented based on the precipitation of serum .beta.-lipoprotein with **sulfated polysaccharides** prior to the LCAT determination. In the absence of .beta.-lipoproteins, more than 7% of serum free **cholesterol** is esterified in the first hour and the reaction rate is linear for about 2 hr. LCAT activities with normal serum expressed as **cholesterol** esterified per .mu.mol/l/hr are lower than the values reported by others. The reason for this discrepancy is that free **cholesterol** specific activity in total serum does not reflect the true specific activity of LCAT **cholesterol** substrate.

CT Medical Descriptors:

in vitro study

theoretical study

normal human

Drug Descriptors:

\***low density lipoprotein**

\*phosphatidylcholine sterol acyltransferase

RN (phosphatidylcholine sterol acyltransferase) 9031-14-5

=> fil medline

FILE 'MEDLINE' ENTERED AT 13:12:16 ON 23 JUN 2001

FILE LAST UPDATED: 18 JUN 2001 (20010618/UP). FILE COVERS 1958 TO DATE.

On April 22, 2001, MEDLINE was reloaded. See HELP RLOAD for details.

MEDLINE now contains new records from the former NLM HEALTH STAR database. These records have an Entry Date and Update Date of 20010223.

MEDLINE thesauri in the /CN, /CT, and /MN fields incorporate the MeSH 2001 vocabulary. Enter HELP THESAURUS for details.

The OLDMEDLINE file segment now contains data from 1958 through 1965. Enter HELP CONTENT for details.

Left, right, and simultaneous left and right truncation are available in the Basic Index. See HELP SFIELDS for details.

THIS FILE CONTAINS CAS REGISTRY NUMBERS FOR EASY AND ACCURATE SUBSTANCE IDENTIFICATION.

=> d all tot 1166

L166 ANSWER 1 OF 5 MEDLINE

AN 91141343 MEDLINE

DN 91141343 PubMed ID: 1899899

TI Pravastatin and simvastatin for hypercholesterolemia.

AU Anonymous

SO MEDICAL LETTER ON DRUGS AND THERAPEUTICS, (1991 Mar 8) 33 (839) 18-20.

Journal code: M52; 2985240R. ISSN: 0025-732X.

CY United States  
DT Journal; Article; (JOURNAL ARTICLE)  
LA English  
FS Abridged Index Medicus Journals; Priority Journals  
EM 199103  
ED Entered STN: 19910412  
Last Updated on STN: 19980206  
Entered Medline: 19910327  
CT Check Tags: Human  
Anticholesteremic Agents: AE, adverse effects  
\*Anticholesteremic Agents: TU, therapeutic use  
Clinical Trials  
Drug Therapy, Combination  
Heptanoic Acids: AE, adverse effects  
\*Heptanoic Acids: TU, therapeutic use  
\*Hypercholesterolemia: DT, drug therapy  
Liver Diseases: CI, chemically induced  
Lovastatin: AE, adverse effects  
\*Lovastatin: AA, analogs & derivatives  
Lovastatin: TU, therapeutic use  
Muscular Diseases: CI, chemically induced  
Naphthalenes: AE, adverse effects  
\*Naphthalenes: TU, therapeutic use  
Pravastatin  
Simvastatin  
RN 75330-75-5 (Lovastatin); 79902-63-9 (Simvastatin); 81093-37-0  
(Pravastatin)  
CN 0 (Anticholesteremic Agents); 0 (Heptanoic Acids); 0 (Naphthalenes)

L166 ANSWER 2 OF 5 MEDLINE  
AN 90072254 MEDLINE  
DN **90072254** PubMed ID: **2589420**  
TI Controlling cholesterol with drugs.  
AU Stoy D B  
CS George Washington University Lipid Research Clinic, Washington, DC.  
SO AMERICAN JOURNAL OF NURSING, (1989 Dec) 89 (12) 1628-31.  
Journal code: 3MW; 0372646. ISSN: 0002-936X.  
CY United States  
DT Journal; Article; (JOURNAL ARTICLE)  
LA English  
FS Abridged Index Medicus Journals; Priority Journals; Nursing Journals  
EM 199001  
ED Entered STN: 19900328  
Last Updated on STN: 19900328  
Entered Medline: 19900105  
CT Check Tags: Human  
\*Anticholesteremic Agents: TU, therapeutic use  
Cholestyramine: TU, therapeutic use  
Drug Therapy, Combination  
\*Hypercholesterolemia: DT, drug therapy  
Lovastatin: TU, therapeutic use  
Niacin: TU, therapeutic use  
RN 11041-12-6 (Cholestyramine); 59-67-6 (Niacin); 75330-75-5 (Lovastatin)  
CN 0 (Anticholesteremic Agents)

L166 ANSWER 3 OF 5 MEDLINE  
AN 88339119 MEDLINE  
DN **88339119** PubMed ID: **3421570**  
TI Lovastatin, nicotinic acid, and rhabdomyolysis.  
AU Reaven P; Witztum J L  
SO ANNALS OF INTERNAL MEDICINE, (1988 Oct 1) 109 (7) 597-8.  
Journal code: 5A6; 0372351. ISSN: 0003-4819.  
CY United States  
DT Letter  
LA English  
FS Abridged Index Medicus Journals; Priority Journals

EM 198810  
ED Entered STN: 19900308  
Last Updated on STN: 19900308  
Entered Medline: 19881025  
CT Check Tags: Case Report; Human; Male  
Adult  
Drug Therapy, Combination  
Hypercholesterolemia, Familial: DT, drug therapy  
\*Lovastatin: AE, adverse effects  
\*Niacin: AE, adverse effects  
\*Rhabdomyolysis: CI, chemically induced  
RN 59-67-6 (Niacin); 75330-75-5 (Lovastatin)

L166 ANSWER 4 OF 5 MEDLINE  
AN 88136074 MEDLINE  
DN **88136074** PubMed ID: **3277742**  
TI HMG-CoA reductase inhibitors. A new approach to the management of hypercholesterolemia.  
AU Cressman M D; Hoogwerf B J; Moodie D S; Olin J W; Weinstein C E  
SO CLEVELAND CLINIC JOURNAL OF MEDICINE, (1988 Jan-Feb) 55 (1) 93-100. Ref: 21  
Journal code: DBN; 8703441. ISSN: 0891-1150.  
CY United States  
DT Journal; Article; (JOURNAL ARTICLE)  
General Review; (REVIEW)  
(REVIEW, TUTORIAL)  
LA English  
FS Priority Journals  
EM 198804  
ED Entered STN: 19900308  
Last Updated on STN: 19900308  
Entered Medline: 19880406  
CT Check Tags: Human  
Colestipol: TU, therapeutic use  
Drug Therapy, Combination  
\*Hydroxymethylglutaryl CoA Reductases: AI, antagonists & inhibitors  
\*Hypercholesterolemia: DT, drug therapy  
Lovastatin: AE, adverse effects  
\*Lovastatin: TU, therapeutic use  
RN 50925-79-6 (Colestipol); 75330-75-5 (Lovastatin)  
CN EC 1.1.1.88 (Hydroxymethylglutaryl CoA Reductases)

L166 ANSWER 5 OF 5 MEDLINE  
AN 88125202 MEDLINE  
DN **88125202** PubMed ID: **3340642**  
TI Lovastatin alone and in combination for treatment of primary hypercholesterolemia.  
AU Stein E A; Lamkin G E; Bewley D Z  
CS Cholesterol Treatment Center, University of Cincinnati Medical Center, Ohio 45267-0714.  
SO PROGRESS IN CLINICAL AND BIOLOGICAL RESEARCH, (1988) 255 281-93.  
Journal code: PZ5; 7605701. ISSN: 0361-7742.  
CY United States  
DT Journal; Article; (JOURNAL ARTICLE)  
LA English  
FS Priority Journals  
EM 198803  
ED Entered STN: 19900308  
Last Updated on STN: 19900308  
Entered Medline: 19880323  
CT Check Tags: Female; Human; Male; Support, Non-U.S. Gov't  
Adult  
Aged  
Anion Exchange Resins: TU, therapeutic use  
Drug Therapy, Combination  
\*Hypercholesterolemia: DT, drug therapy



Hypercholesterolemia, Familial: DT, drug therapy  
 Lipoproteins, HDL Cholesterol: BL, blood  
 Lipoproteins, LDL Cholesterol: BL, blood  
 Lovastatin: AE, adverse effects  
 \*Lovastatin: TU, therapeutic use  
 Middle Age  
 Niacin: TU, therapeutic use  
 Patient Compliance

RN 59-67-6 (Niacin); 75330-75-5 (Lovastatin)  
 CN 0 (Anion Exchange Resins); 0 (Lipoproteins, HDL Cholesterol); 0  
 (Lipoproteins, LDL Cholesterol)

=> d all tot 1173

L173 ANSWER 1 OF 63 MEDLINE

AN 95196837 MEDLINE

DN 95196837 PubMed ID: 7890014

TI The effect of probucol and vitamin E treatment on the oxidation of  
 low-density lipoprotein and forearm vascular responses in humans.

AU McDowell I F; Brennan G M; McEneny J; Young I S; Nicholls D P; McVeigh G  
 E; Bruce I; Trimble E R; Johnston G D

CS Department of Clinical Biochemistry, Queen's University, Royal Victoria  
 Hospital, Belfast, Northern Ireland.

SO EUROPEAN JOURNAL OF CLINICAL INVESTIGATION, (1994 Nov) 24 (11)  
 759-65.

Journal code: EN3; 0245331. ISSN: 0014-2972.

CY ENGLAND: United Kingdom

DT (CLINICAL TRIAL)

Journal; Article; (JOURNAL ARTICLE)

(RANDOMIZED CONTROLLED TRIAL)

LA English

FS Priority Journals

EM 199504

ED Entered STN: 19950427

Last Updated on STN: 19980206

Entered Medline: 19950414

AB This study investigates the hypothesis that lipid soluble antioxidants may  
 increase the resistance of low-density lipoprotein (LDL) to oxidation and  
 also enhance vascular endothelial responses in humans. In a double-blind  
 parallel group study, 24 **hypercholesterolaemic** patients already  
 on treatment with simvastatin (20 mg day<sup>-1</sup>), were randomized to  
 supplementary treatment with probucol (500 mg bd), vitamin E (400 IU  
 daily) or placebo for 8 weeks. Mean serum **cholesterol** before  
 antioxidant treatment was 7.00 mmol l<sup>-1</sup>. Resistance of LDL to oxidation by  
 copper was increased by 830% in the probucol group and by 30% in the  
 vitamin E group. However, thiobarbituric acid reacting substances in whole  
 serum were not altered by either antioxidant. Probucol lowered HDL- and  
 LDL-**cholesterol** levels and increased the QT interval. Forearm  
 vascular responses, as measured by venous occlusion plethysmography, to  
 acetylcholine, glyceryl trinitrate and NG-monomethyl-L-arginine, were not  
 significantly changed by antioxidant treatment. Probucol has a major, and  
 vitamin E a minor, effect on LDL resistance to oxidation but neither  
 compound appears to alter forearm vascular responses in vivo.

CT Check Tags: Female; Human; Male; Support, Non-U.S. Gov't

Adult

Antilipemic Agents: AD, administration & dosage

Double-Blind Method

Drug Administration Schedule

**Drug Therapy, Combination**

\*Forearm: BS, blood supply

**Hyperlipidemia: BL, blood**

\***Hyperlipidemia: DT, drug therapy**

\***Lipoproteins, LDL Cholesterol: BL, blood**

**Lipoproteins, LDL Cholesterol: DE, drug effects**

**Lovastatin: AD, administration & dosage**

**Lovastatin: AA, analogs & derivatives**  
 Middle Age  
 Oxidation-Reduction: DE, drug effects  
**\*Probucol: AD, administration & dosage**  
**Probucol: AE, adverse effects**  
 Regional Blood Flow

**Simvastatin**

\*Vitamin E: AD, administration & dosage  
 Vitamin E: AE, adverse effects  
 Vitamin E: BL, blood

RN 1406-18-4 (Vitamin E); 23288-49-5 (Probucol); 75330-75-5  
 (Lovastatin); 79902-63-9 (Simvastatin)  
 CN 0 (Antilipemic Agents); 0 (Lipoproteins, LDL Cholesterol)

L173 ANSWER 2 OF 63 MEDLINE

AN 95181606 MEDLINE

DN 95181606 PubMed ID: 7876371

TI Dual bezafibrate-simvastatin therapy for combined hyperlipidaemia.

AU Hutchesson A C; Moran A; Jones A F

CS Department of Clinical Chemistry, Birmingham Heartlands Hospital,  
 Bordesley Green East, U.K.

SO JOURNAL OF CLINICAL PHARMACY AND THERAPEUTICS, (1994 Dec) 19 (6)  
 387-9.

Journal code: HPI; 8704308. ISSN: 0269-4727.

CY ENGLAND: United Kingdom

DT Journal; Article; (JOURNAL ARTICLE)

LA English

FS Priority Journals

EM 199504

ED Entered STN: 19950419

Last Updated on STN: 19980206

Entered Medline: 19950406

AB Statins and fibrates are both effective in the treatment of  
 hyperlipidaemias but are not recommended in combination because episodes  
 of rhabdomyolysis have followed combined **lovastatin**-gemfibrozil  
 therapy. We assessed treatment with dual bezafibrate-simvastatin therapy  
 in routine clinical practice. In 22 patients, total **cholesterol**,  
 LDL-**cholesterol** and triglycerides fell by 20.1% (P < 0.0001),  
 35.1% (P < 0.001) and 31% (P < 0.05) respectively, and HDL-  
**cholesterol** rose by 18.4% (P < 0.05) on combination therapy. The  
 reduction in **cholesterol** followed the introduction of  
 simvastatin, while the decrease in triglycerides followed treatment with  
 bezafibrate. No patient developed myopathy. We conclude that dual  
 simvastatin-bezafibrate therapy is well tolerated and may reduce  
 triglyceride concentrations, but offers no advantage in  
**cholesterol** reduction over treatment with simvastatin alone.

CT Check Tags: Female; Human; Male

Adult

Aged

\*Antilipemic Agents: TU, therapeutic use

\*Bezafibrate: TU, therapeutic use

Cholesterol: BL, blood

Drug Therapy, Combination

Hyperlipidemia: BL, blood

\*Hyperlipidemia: DT, drug therapy

Lipoproteins, HDL Cholesterol: BL, blood

Lipoproteins, LDL Cholesterol: BL, blood

\*Lovastatin: AA, analogs & derivatives

Lovastatin: TU, therapeutic use

Middle Age

**Simvastatin**

Triglycerides: BL, blood

RN 41859-67-0 (Bezafibrate); 57-88-5 (Cholesterol); 75330-75-5  
 (Lovastatin); 79902-63-9 (Simvastatin)

CN 0 (Antilipemic Agents); 0 (Lipoproteins, HDL Cholesterol); 0  
 (Lipoproteins, LDL Cholesterol); 0 (Triglycerides)

L173 ANSWER 3 OF 63 MEDLINE

AN 95171622 MEDLINE

DN 95171622 PubMed ID: 7867225

TI HBPRCA Astra Award. Therapeutic restoration of endothelial function in **hypercholesterolaemic** subjects: effect of fish oils.

AU Chin J P; Dart A M

CS Alfred and Baker Medical Unit, Baker Medical Research Institute, Prahan, Victoria, Australia.

SO CLINICAL AND EXPERIMENTAL PHARMACOLOGY AND PHYSIOLOGY, (1994 Oct) 21 (10) 749-55.

Journal code: DD8; 0425076. ISSN: 0305-1870.

CY Australia

DT (CLINICAL TRIAL)

(CONTROLLED CLINICAL TRIAL)

Journal; Article; (JOURNAL ARTICLE)

LA English

FS Priority Journals

EM 199503

ED Entered STN: 19950407

Last Updated on STN: 19980206

Entered Medline: 19950329

AB 1. Endothelial dysfunction, evidenced as an impaired response to acetylcholine, is well documented in **hypercholesterolaemic** subjects. We examined the ability of dietary supplementation with fish oils to restore endothelial function in forearm resistance vessels in these patients and compared this with restoration by lipid-lowering therapy. 2. Responses of forearm blood flow to acetylcholine (4.6, 9.25, 18.5 and 37 micrograms/min) and sodium nitroprusside (200, 400, 800 and 1600 ng/min) were obtained using forearm venous occlusion plethysmography in nine **hypercholesterolaemic** and seven age-matched control subjects. The dose-response curve to acetylcholine was significantly blunted in **hypercholesterolaemic** subjects when compared with controls ( $P < 0.001$ ). Responses to sodium nitroprusside were not different between the two groups ( $P = 0.37$ ). 3. Lipid-lowering therapy decreased total plasma **cholesterol** levels by 33% and significantly augmented the responses to acetylcholine ( $P = 0.001$ ) but not to sodium nitroprusside in the **hypercholesterolaemic** subjects. 4. Dietary supplementation with fish oils had no effect on either total or low density lipoprotein-**cholesterol** but significantly augmented the responses to acetylcholine ( $P = 0.011$ ) in **hypercholesterolaemic** subjects. Responses to sodium nitroprusside were not altered ( $P = 0.94$ ). 5. This study shows that endothelium-dependent relaxation is impaired in subjects with high **cholesterol** levels and that this impairment can be reversed by lowering low density lipoproteins (LDL) **cholesterol** levels. In addition, we demonstrate that restoration of endothelial function can occur without changes in LDL levels, by dietary supplementation with fish oils.

CT Check Tags: Female; Human; Male

Acetylcholine: PD, pharmacology

Adult

Australia

Awards and Prizes

**Cholesterol: BL, blood**

**Cholestyramine: TU, therapeutic use**

**Drug Therapy, Combination**

\*Endothelium, Vascular: DE, drug effects

\*Fish Oils: TU, therapeutic use

Forearm: BS, blood supply

\***Hypercholesterolemia: DH, diet therapy**

Hypertension

**Lipoproteins, LDL Cholesterol: BL, blood**

**Lovastatin: AA, analogs & derivatives**

**Lovastatin: TU, therapeutic use**

Middle Age

Regional Blood Flow: DE, drug effects

**Simvastatin**

RN 11041-12-6 (Cholestyramine); 51-84-3 (Acetylcholine);  
57-88-5 (Cholesterol); 75330-75-5 (Lovastatin);  
79902-63-9 (Simvastatin)  
CN 0 (Fish Oils); 0 (Lipoproteins, LDL Cholesterol)

L173 ANSWER 4 OF 63 MEDLINE

AN 95154373 MEDLINE

DN 95154373 PubMed ID: 7851467

TI Postprandial apolipoprotein B100 and B48 metabolism in familial combined hyperlipidaemia before and after reduction of fasting plasma triglycerides.

AU Castro Cabezas M; Erkelens D W; Kock L A; De Bruin T W

CS Department of Internal Medicine, University Hospital, Utrecht, The Netherlands.

SO EUROPEAN JOURNAL OF CLINICAL INVESTIGATION, (1994 Oct) 24 (10) 669-78.

Journal code: EN3; 0245331. ISSN: 0014-2972.

CY ENGLAND: United Kingdom

DT Journal; Article; (JOURNAL ARTICLE)

LA English

FS Priority Journals

EM 199503

ED Entered STN: 19950322

Last Updated on STN: 19980206

Entered Medline: 19950313

AB Hepatic VLDL overproduction in familial combined hyperlipidaemia (FCH) may delay the clearance of atherogenic apolipoprotein (apo) B containing particles. We investigated if normalization of fasting plasma triglycerides (TG) by hypolipidaemic treatment results in improved metabolism of apo B48 and apo B100 in six male subjects with FCH and compared them to six normolipidaemic controls. The FCH patients were studied before (TG, 5.2 +/- 1.2 mmol l<sup>-1</sup>; mean +/- SEM) and after therapy (TG, 2.1 +/- 0.3 mmol l<sup>-1</sup>) with either simvastatin (n = 4) or combined therapy with gemfibrozil (n = 2). The postprandial changes of apo B100 and apo B48 were studied after a single oral fat meal (24 h; 50 gram fat m<sup>-2</sup>). Changes in triglyceride rich particles (TRP; d < 1.006 g ml<sup>-1</sup>) and remnant fractions (REM; d:1.006-1.019 g ml<sup>-1</sup>) of apo B were quantitated by scanning silverstained SDS-PAGE (4-15%). Apo B48 in fasting TRP in untreated and treated FCH was 15% and 14% of total apo B, and 6% in controls (P < 0.05). In controls, postprandial B48 increased maximally at 4 h by 81% in TRP and by 137% in REM compared to baseline. In treated FCH, the postprandial apo B48 pattern normalized in TRP compared to the untreated state. Postprandial apo B100 in controls decreased in TRP and REM by 33% and 18% (P < 0.05). In untreated and treated FCH, postprandial apo B100 remained unchanged vs. baseline in TRP and in REM suggesting hypersecretion of VLDL. The elimination of B100--assessed as area under the curve--in TRP (32.5 +/- 3.6 au.h; mean +/- SEM) and REM fractions (33.2 +/- 3.1 au.h), improved significantly after treatment (21.0 +/- 2.8 and 20.4 +/- 3.3 au.h, respectively). The apo B48 clearance in TRP fractions was improved after treatment (4.3 +/- 1.4 au.h vs. 2.9 +/- 1.2 au.h; P = 0.06), but not in REM fractions (2.8 +/- 1.0 au.h vs. 1.8 +/- 0.5 au.h; NS). In conclusion, in FCH subjects with apo B100 hypersecretion and increased fasting plasma apo B48 levels, reduction of fasting plasma TG improved, but did not normalize, TRP apo B48 and B100 metabolism. However, therapy normalized postprandial apo B100 remnant metabolism. Impaired postprandial apo B metabolism may be instrumental in the development of premature atherosclerosis in FCH subjects.

CT Check Tags: Female; Human; Male; Support, Non-U.S. Gov't

Adult

Aged

\*Apolipoproteins B: ME, metabolism

Child

Cholesterol: BL, blood

Drug Therapy, Combination

Fasting

\*Gemfibrozil: AD, administration & dosage  
 Hyperlipidemia, Familial Combined: BL, blood  
 Hyperlipidemia, Familial Combined: DT, drug therapy  
 \*Hyperlipidemia, Familial Combined: ME, metabolism  
 Lovastatin: AD, administration & dosage  
 \*Lovastatin: AA, analogs & derivatives

Middle Age

Simvastatin

\*Triglycerides: BL, blood

RN 25812-30-0 (Gemfibrozil); 57-88-5 (Cholesterol); 75330-75-5 (Lovastatin); 79902-63-9 (Simvastatin)

CN 0 (Apolipoproteins B); 0 (Triglycerides); 0 (apolipoprotein B-100); 0 (apolipoprotein B-48)

L173 ANSWER 5 OF 63 MEDLINE

AN 95066045 MEDLINE

DN 95066045 PubMed ID: 7975581

TI [Effect of combined treatment with **lovastatin** and colestipol on serum lipids and lipoproteins].

Wplyw skojarzonego leczenia **lovastatinem** i kolestipolem na lipidy i lipoproteiny surowicy.

AU Klosiewicz-Latoszek L; Nowicka G; Szostak W B

CS Zakladu Zywienia Klinicznego Instytutu Zywnosci i Zywienia w Warszawie.

SO WIADOMOSCI LEKARSKIE, (1993 Aug) 46 (15-16) 581-5.

Journal code: XOA; 9705467. ISSN: 0043-5147.

CY Poland

DT Journal; Article; (JOURNAL ARTICLE)

LA Polish

FS Priority Journals

EM 199412

ED Entered STN: 19950110

Last Updated on STN: 19950110

Entered Medline: 19941215

AB In 20 men with **hypercholesterolaemia** or mixed hyperlipaemia the effect was evaluated of treatment with **Lovastatin** and Colestipol on lipoproteins. Administration of the drugs in combination or alone decreased significantly the concentrations of total **cholesterol** (TC), LDL **cholesterol** (LDL-chol), and apolipoprotein B (apo B). The combination of **Lovastatin** in dose of 40 mg with Colestipol in dose of 10 g decreased more favourably the concentrations of TC (34.7%), LDL-chol (44.3%), and apo B (22.4%) than administration of each of the drugs alone in higher doses i.e. **Lovastatin** 80 mg (TC--26.8%, LDL-chol--31.8%, apo B--16.9%) or Colestipol 20 g (TC -20.0%, LDL-chol-26.3%, apo B-10.8%). The treatment with **Lovastatin** and Colestipol failed to change significantly the concentrations of triglycerides, HDL **cholesterol** and AI and AII apolipoproteins. The combined therapy was better tolerated than monotherapy.

CT Check Tags: Human; Male

Adult

Aged

\*Colestipol: TU, therapeutic use

Drug Therapy, Combination

\*Hypercholesterolemia: DT, drug therapy

\*Hyperlipidemia: DT, drug therapy

Lipids: BL, blood

Lipoproteins: BL, blood

\*Lovastatin: TU, therapeutic use

Middle Age

RN 50925-79-6 (Colestipol); 75330-75-5 (Lovastatin)

CN 0 (Lipids); 0 (Lipoproteins)

L173 ANSWER 6 OF 63 MEDLINE

AN 94265237 MEDLINE

DN 94265237 PubMed ID: 8205598

TI Therapeutic use of **lovastatin** in the treatment of **hypercholesterolemia**.

AU Illingworth D R  
CS Department of Medicine, Oregon Health Sciences University, Portland.  
NC HL28399 (NHLBI)  
P30DK40566 (NIDDK)  
RR334 (NCRR)  
SO CLINICAL THERAPEUTICS, (1994 Jan-Feb) 16 (1) 2-26; discussion 1.  
Ref: 66  
Journal code: CPE; 7706726. ISSN: 0149-2918.  
CY United States  
DT Journal; Article; (JOURNAL ARTICLE)  
General Review; (REVIEW)  
(REVIEW, TUTORIAL)  
LA English  
FS Priority Journals  
EM 199407  
ED Entered STN: 19940721  
Last Updated on STN: 19940721  
Entered Medline: 19940708  
AB The present review discusses the mechanism of action, efficacy, safety profile, and potential uses of **lovastatin** in patients with **hypercholesterolemia**. Data on the efficacy of **lovastatin** are evaluated in different patient populations; also, the efficacy of this agent in the long-term treatment of patients followed by the author is presented. No new safety concerns have emerged during long-term treatment of selected patients with **lovastatin**, and, in compliant patients, hypolipidemic effects are maintained during continuous treatment with therapy that exceeds 5 years. On the basis of available data, **lovastatin** should be regarded as one of the drugs of first choice in the treatment of adult patients with **hypercholesterolemia** and increased plasma concentrations of low-density lipoproteins.  
CT Check Tags: Human; Support, U.S. Gov't, P.H.S.  
Drug Therapy, Combination  
Hydroxymethylglutaryl CoA Reductases: AI, antagonists & inhibitors  
\*Hypercholesterolemia: DT, drug therapy  
Hypercholesterolemia: ME, metabolism  
Hyperlipidemia: DT, drug therapy  
Hyperlipidemia: ME, metabolism  
Lipoproteins: ME, metabolism  
Lipoproteins, LDL Cholesterol: BL, blood  
Lovastatin: AE, adverse effects  
Lovastatin: CH, chemistry  
Lovastatin: ME, metabolism  
\*Lovastatin: TU, therapeutic use  
Triglycerides: BL, blood  
RN 75330-75-5 (Lovastatin)  
CN 0 (Lipoproteins); 0 (Lipoproteins, LDL Cholesterol); 0 (Triglycerides); EC 1.1.1.88 (Hydroxymethylglutaryl CoA Reductases)  
L173 ANSWER 7 OF 63 MEDLINE  
AN 94066432 MEDLINE  
DN 94066432 PubMed ID: 7504129  
TI Long-term treatment (2 years) with the HMG CoA reductase inhibitors **lovastatin** or pravastatin in combination with **cholestyramine** in patients with severe primary **hypercholesterolemia**.  
AU Jacob B G; Richter W O; Schwandt P  
CS Department of Medicine II, University of Munich, Germany.  
SO JOURNAL OF CARDIOVASCULAR PHARMACOLOGY, (1993 Sep) 22 (3) 396-400.  
Journal code: K78; 7902492. ISSN: 0160-2446.  
CY United States  
DT Journal; Article; (JOURNAL ARTICLE)  
LA English  
FS Priority Journals  
EM 199401  
ED Entered STN: 19940201

Last Updated on STN: 19960129

Entered Medline: 19940104

AB The effects of the two HMG CoA reductase inhibitors **lovastatin** and pravastatin in combination with 12-16 g **cholestyramine** on serum lipids were studied in 18 patients with severe primary **hypercholesterolemia**. Combined therapy of **cholestyramine** with **lovastatin** (80 mg daily) decreased low-density-lipoprotein (LDL) **cholesterol** by 44% (baseline 7.65 +/- 0.51 mM) and increased high-density-lipoprotein (HDL) **cholesterol** by 20% (baseline 1.22 +/- 0.12 mM) in 9 patients after 2 years. In 9 other patients with comparable baseline lipid values, **cholestyramine** plus pravastatin (40 mg daily) reduced LDL **cholesterol** to a comparable extent after 2 years (-43%, baseline 7.71 +/- 0.44 mM) and increased HDL **cholesterol** by 18% (baseline 1.06 +/- 0.11 mM). The combination with **lovastatin** led to a significant reduction in triglycerides level by 25% (baseline 1.63 +/- 0.24 mM), whereas the combination with pravastatin did not change triglycerides level (baseline 1.39 +/- 0.15 mM). Both drug regimens were well tolerated without serious side effects. The effects of both HMG CoA reductase inhibitors after 2 years were comparable to those after short-term intake and after 1-year therapy without loss of efficacy.

CT Check Tags: Female; Human; Male

Adult

Aged

**Cholestyramine: AD, administration & dosage**

**\*Cholestyramine: TU, therapeutic use**

**Drug Therapy, Combination**

**\*Hypercholesterolemia: DT, drug therapy**

**Lipoproteins, HDL Cholesterol: BL, blood**

**Lipoproteins, LDL Cholesterol: BL, blood**

**Lovastatin: AD, administration & dosage**

**\*Lovastatin: TU, therapeutic use**

Middle Age

**Pravastatin: AD, administration & dosage**

**\*Pravastatin: TU, therapeutic use**

Triglycerides: BL, blood

RN 11041-12-6 (**Cholestyramine**); 75330-75-5 (**Lovastatin**);

81093-37-0 (**Pravastatin**)

CN 0 (**Lipoproteins, HDL Cholesterol**); 0 (**Lipoproteins, LDL Cholesterol**); 0 (**Triglycerides**)

L173 ANSWER 8 OF 63 MEDLINE

AN 94030808 MEDLINE

DN 94030808 PubMed ID: 8217032

TI Effect and tolerability of combining **lovastatin** with nifedipine or lisinopril.

AU Os I; Bratland B; Dahlof B; Gisholt K; Syvertsen J O; Tretli S

CS Department of Nephrology, Ulleval University Hospital, Oslo, Norway.

SO AMERICAN JOURNAL OF HYPERTENSION, (1993 Aug) 6 (8) 688-92.

Journal code: AJI; 8803676. ISSN: 0895-7061.

CY United States

DT (CLINICAL TRIAL)

Journal; Article; (JOURNAL ARTICLE)

(RANDOMIZED CONTROLLED TRIAL)

LA English

FS Priority Journals

EM 199312

ED Entered STN: 19940117

Last Updated on STN: 19940117

Entered Medline: 19931203

AB Single cardiovascular risk factor intervention is probably not sufficient to prevent atherosclerosis progression. There is a lack of data on concomitant use of **hypocholesterolemic** agents and antihypertensive drugs with respect to possible interactions and adverse experiences. We studied 293 patients (below 65 years of age) under treatment with either lisinopril (n = 144) or nifedipine (n = 149) for

mild to moderate hypertension for 10 weeks, and with serum **cholesterol** above 6.5 mmol/L, who were randomized to either **lovastatin** 20 mg every day or placebo in a double-blind, double-dummy design for 6 weeks. **Lovastatin** effectively lowered **cholesterol** by 16% and 15% in the lisinopril and nifedipine group respectively ( $P < .01$  compared to placebo for both groups) without any negative impact on the antihypertensive efficacy of either lisinopril or nifedipine. The drugs in combination were well tolerated and did not affect the well-being of the patients, and did not cause any more adverse effects than the antihypertensive agents alone. Liver enzymes increased slightly during **lovastatin** therapy, while no case of myopathy was reported. Combined therapy with **lovastatin** and antihypertensive therapy can be safely undertaken.

CT Check Tags: Female; Human; Male; Support, Non-U.S. Gov't  
Double-Blind Method  
Drug Interactions

**Drug Therapy, Combination**

\*Hypercholesterolemia: DT, drug therapy

\*Hypertension: DT, drug therapy

Lisinopril: AE, adverse effects

\*Lisinopril: TU, therapeutic use

**Lovastatin: AE, adverse effects**

\***Lovastatin: TU, therapeutic use**

Middle Age

Nifedipine: AE, adverse effects

\*Nifedipine: TU, therapeutic use

Quality of Life

Risk Factors

RN 21829-25-4 (Nifedipine); 75330-75-5 (**Lovastatin**); 83915-83-7  
(Lisinopril)

L173 ANSWER 9 OF 63 MEDLINE

AN 94023770 MEDLINE

DN 94023770 PubMed ID: 8210967

TI Effectiveness of low-dose **lovastatin** combined with low-dose colestipol in moderate to severe primary **hypercholesterolaemia**.

AU Tonstad S; Ose L; Gorbitz C; Harrison E M; de Koning Gans H J

CS Department of Medicine A, Rikshospitalet, Oslo, Norway.

SO SCANDINAVIAN JOURNAL OF CLINICAL AND LABORATORY INVESTIGATION, (1993 Aug) 53 (5) 457-63.

Journal code: UCP; 0404375. ISSN: 0036-5513.

CY ENGLAND: United Kingdom

DT (CLINICAL TRIAL)

Journal; Article; (JOURNAL ARTICLE)

(RANDOMIZED CONTROLLED TRIAL)

LA English

FS Priority Journals

EM 199311

ED Entered STN: 19940117

Last Updated on STN: 19950206

Entered Medline: 19931105

AB The effect of the combination of low-dose **lovastatin** and low-dose colestipol was studied among 57 subjects with moderate to severe primary **hypercholesterolaemia** (total **cholesterol**  $>$  or  $= 7.0$  mmol l<sup>-1</sup>). Following an 8-week dietary phase, participants were randomized to treatment with 20 mg of **lovastatin** combined with 5 g or with 10 g of colestipol, or to matching placebo. Baseline total **cholesterol** was  $7.7 \pm 0.9$  mmol l<sup>-1</sup> after dietary stabilization. Total **cholesterol** levels were reduced to  $5.6 \pm 0.7$  mmol l<sup>-1</sup> and  $5.8 \pm 0.7$  mmol l<sup>-1</sup> after 4 and 8 weeks of treatment in the **lovastatin** 5 g-1 colestipol group, and 74% of the subjects achieved the goal of low density lipoprotein (LDL) **cholesterol** levels of  $>$  or  $= 4.0$  mmol l<sup>-1</sup>. Among the **lovastatin** 10 g-1 colestipol group, total **cholesterol** was reduced to  $5.4 \pm 0.5$  mmol l<sup>-1</sup> and  $5.5 \pm 0.9$  mmol l<sup>-1</sup> following 4 and 8 weeks, and 80% of subjects achieved the LDL **cholesterol** goal. No change was seen



in the placebo group. Thus, low-dose combination therapy with **lovastatin** and colestipol, in conjunction with dietary treatment, is effective in moderate to severe primary **hypercholesterolaemia**, and is well tolerated.

CT Check Tags: Female; Human; Male

Adult

Aged

**Cholesterol: BL, blood**

\*Colestipol: AD, administration & dosage

Colestipol: AE, adverse effects

**Drug Therapy, Combination**

Hydroxymethylglutaryl CoA Reductases: AI, antagonists & inhibitors

\***Hypercholesterolemia: DT, drug therapy**

\***Lovastatin: AD, administration & dosage**

**Lovastatin: AE, adverse effects**

Middle Age

RN 50925-79-6 (Colestipol); 57-88-5 (Cholesterol); 75330-75-5

(**Lovastatin**)

CN EC 1.1.1.88 (Hydroxymethylglutaryl CoA Reductases)

L173 ANSWER 10 OF 63 MEDLINE

AN 93326083 MEDLINE

DN 93326083 PubMed ID: 8333817

TI Combination drug therapy for **hypercholesterolemia**. The trade-off between cost and simplicity.

AU Heudebert G R; Van Ruiswyk J; Hiatt J; Schectman G

CS Department of Medicine, Medical College of Wisconsin, Zablocki Veterans Affairs Medical Center, Milwaukee.

SO ARCHIVES OF INTERNAL MEDICINE, (1993 Aug 9) 153 (15) 1828-37.

Journal code: 7FS; 0372440. ISSN: 0003-9926.

CY United States

DT Journal; Article; (JOURNAL ARTICLE)

LA English

FS Abridged Index Medicus Journals; Priority Journals

EM 199308

ED Entered STN: 19930826

Last Updated on STN: 19930826

Entered Medline: 19930819

AB BACKGROUND: The National **Cholesterol** Education Program recommends achievement of a defined target level of low-density lipoprotein **cholesterol** (LDL-C) for the treatment of **hypercholesterolemia**. They endorse the use of niacin and/or sequestrants as the first line of therapy to achieve such target LDL-C level. This recommendation has not been compared with the use of **lovastatin** as initial therapy if multidrug regimens are required to achieve goal LDL-C. METHODS: Prospectively collected data on tolerance and effectiveness for niacin, sequestrants, and **lovastatin** were obtained from a lipid clinic at a large midwestern Veterans Affairs medical center. We used a decision tree to compare the complexity and cost of three sequential drug algorithms used for the following initial LDL-C levels: 4.14, 4.91, 5.69, and 6.47 mmol/L (160, 190, 220, and 250 mg/dL). Algorithm 1 was niacin followed by a sequestrant and then **lovastatin**; algorithm 2, a sequestrant followed by niacin and then **lovastatin**; and algorithm 3, **lovastatin** followed by niacin and a sequestrant. Drug and laboratory costs were obtained from the pharmacy and pathology services at the same institution. Sensitivity analyses were performed on the tolerance and effectiveness of each drug as well as drug and laboratory cost estimates. RESULTS: The probability of achieving target LDL-C level (3.36 mmol/L [130 mg/dL]) decreased as initial LDL-C level increased. As a rule, algorithm 3 required fewer drugs in combination to achieve the target level for all initial LDL-C levels modeled. In addition, the use of **lovastatin** was high across all algorithms at all initial LDL-C levels modeled. Algorithm 1 was less expensive than algorithm 2 or 3 at a low initial LDL-C level (4.14 mmol/L [160 mg/dL]), with an average cost of \$375 vs \$454 vs \$585, respectively. At all other initial LDL-C levels (4.91, 5.69, and 6.47 mmol/L [190, 220,

and 250 mg/dL]), algorithm 2 was slightly less expensive than algorithm 1. Algorithm 3 became relatively less expensive as initial LDL-C level increased: 56% more expensive than algorithm 1 at an initial LDL-C level of 4.14 mmol/L (160 mg/dL) as compared with 7% more expensive than algorithm 1 at an initial LDL-C level of 6.47 mmol/L (250 mg/dL). CONCLUSIONS: Fulfillment of the target LDL-C approach recommended by the National Cholesterol Education Program often requires the use of multiple drugs. When **lovastatin** is used initially, the regimen becomes simpler, albeit more expensive. At initial LDL-C levels of 4.91 mmol/L (190 mg/dL) or higher, this difference in cost becomes progressively smaller (7% at 6.47 mmol/L [250 mg/dL]), making algorithm 3 the better alternative; at low initial LDL-C levels (4.14 mmol/L [160 mg/dL]), a niacin-first regimen is reasonably simple and substantially less expensive. At moderate and severe initial LDL-C levels (4.91 and 5.69 mmol/L [190 and 220 mg/dL]), the **lovastatin**-first regimen may be advantageous.

CT Check Tags: Female; Human; Male; Support, U.S. Gov't, Non-P.H.S.

Aged

Algorithms

\***Anticholesteremic Agents: AD, administration & dosage**

**Anticholesteremic Agents: EC, economics**

Decision Trees

Drug Costs

**Drug Therapy, Combination**

Hospitals, Veterans

\***Hypercholesterolemia: DT, drug therapy**

**Hypercholesterolemia: EC, economics**

**Lovastatin: TU, therapeutic use**

Middle Age

Midwestern United States

Niacin: TU, therapeutic use

Probability

Prospective Studies

Treatment Outcome

RN 59-67-6 (Niacin); 75330-75-5 (**Lovastatin**)

CN 0 (**Anticholesteremic Agents**)

L173 ANSWER 11 OF 63 MEDLINE

AN 93321450 MEDLINE

DN 93321450 PubMed ID: 8330475

TI Evidence of combined therapy of dyslipoproteinemia by HMG-CoA reductase inhibitors and "essential" phospholipids.

AU Gurevich V S; Bondarenko B B; Mikhailova I A; Kasennova N I; Popov Yu G; Astashkina; Le Van Thach T D

CS Cardiology Institute, S. Petersburg, Russia.

SO CLINICA TERAPEUTICA, (1993 Apr) 142 (4) 329-34.

Journal code: DKN; 0372604. ISSN: 0009-9074.

CY Italy

DT Journal; Article; (JOURNAL ARTICLE)

LA English

FS Priority Journals

EM 199308

ED Entered STN: 19930826

Last Updated on STN: 19930826

Entered Medline: 19930819

AB Platelets are involved in the initiation of atheromas and arterial thrombosis and thus may play a cardinal role in the pathogenesis of myocardial and cerebral infarction. In 18 patients with coronary artery disease and **hypercholesterolemia** resistant to low-lipid diet a 12 week treatment with **lovastatin** (HMG-CoA reductase inhibitor) leads to the reduction of total **cholesterol**, LDL-**cholesterol** and triglycerides but also to a marked increase of platelet activity. **Lovastatin** is an inactive lacton prodrug which must be enzymatically or chemically transformed to the active form. In in-vitro experiments, it was discovered that both chemically hydrolysed **lovastatin** and plasma containing **lovastatin** metabolites

stimulate induced platelet aggregation in whole blood samples. "Essential" phospholipids (Lipostabil) added to the blood samples in concentrations according to those which are used clinically prevent this stimulation. This corresponds to data obtained earlier from Lipostabil-treated ischemic heart disease patients. Besides a lipid-lowering effect Lipostabil showed a 50% reduction of spontaneous aggregates in plasma, an increase of the susceptibility threshold to aggregation inducers and a decrease of the platelet aggregation amplitude in whole blood samples. Therefore, it would be promising to combine the therapy by **lovastatin** with "essential" phospholipids possessing a remarkable improving effect on the platelet function based on a molecular action independent of their moderate lipid-reducing action.

CT Check Tags: Human; Male  
Adult

Cholesterol: BL, blood

Coronary Disease: BL, blood

\*Coronary Disease: DT, drug therapy

Drug Therapy, Combination

Hypercholesterolemia: BL, blood

\*Hypercholesterolemia: DT, drug therapy

Lipoproteins, LDL: BL, blood

\*Lovastatin: TU, therapeutic use

Phosphatidylcholines: PD, pharmacology

\*Phosphatidylcholines: TU, therapeutic use

Platelet Aggregation: DE, drug effects

RN 11096-62-1 (lipostabil); 57-88-5 (Cholesterol); 75330-75-5 (Lovastatin)

CN 0 (Lipoproteins, LDL); 0 (Phosphatidylcholines)

L173 ANSWER 12 OF 63 MEDLINE

AN 93299805 MEDLINE

DN 93299805 PubMed ID: 8519043

TI Treatment of severe, resistant familial combined hyperlipidemia with a bezafibrate-**lovastatin** combination.

AU Yeshurun D; Abukarshin R; Elias N; Lanir A; Naschitz J E

CS Department of Medicine A, B'nai Zion Medical Center, Technion, Haifa, Israel.

SO CLINICAL THERAPEUTICS, (1993 Mar-Apr) 15 (2) 355-63.

Journal code: CPE; 7706726. ISSN: 0149-2918.

CY United States

DT Journal; Article; (JOURNAL ARTICLE)

LA English

FS Priority Journals

EM 199307

ED Entered STN: 19930813

Last Updated on STN: 19930813

Entered Medline: 19930726

AB Familial combined hyperlipidemia (FCHL) is a common lipid disorder characterized by high levels of **cholesterol**, triglycerides, or both. The basic metabolic abnormality is overproduction of apolipoprotein B-100. High atherogenicity has been attributed to all forms of FCHL. We evaluated combined bezafibrate-**lovastatin** therapy in 10 patients (9 men and 1 woman) with FCHL and markedly high **cholesterol** and triglyceride levels who were at high risk of coronary artery disease and who had not responded to diet and bezafibrate treatment alone. Eight patients had coronary artery disease, 6 had hypertension, and 3 had noninsulin-dependent diabetes mellitus. **Lovastatin** 20 mg/day was added to the bezafibrate 600 mg/day regimen for 6 weeks; the **lovastatin** dosage was then doubled to 40 mg/day for an additional 6 weeks. The addition of 20 mg of **lovastatin** resulted in decreases of 15%, 20%, and 13% in total **cholesterol**, low-density lipoprotein (LDL) **cholesterol**, and triglyceride levels, respectively. Increasing the dose of **lovastatin** to 40 mg resulted in further moderate decreases of 4%, 3%, and 8% in total **cholesterol**, LDL **cholesterol**, and triglycerides, respectively, compared with the 20 mg/day dosage. Although previous

reports have emphasized the potential side effects of combination treatment with **lovastatin** and fibric acid derivatives, our patients tolerated the regimen well, with no significant subjective complaints or laboratory abnormalities. The bezafibrate-**lovastatin** combination is a possible therapeutic option for severe, resistant FCHL, but close medical supervision is needed because of potential side effects.

CT Check Tags: Female; Human; Male

Adult

Bezafibrate: AD, administration & dosage

Bezafibrate: AE, adverse effects

\*Bezafibrate: TU, therapeutic use

Cholesterol: BL, blood

Drug Resistance

Drug Therapy, Combination

\*Hyperlipidemia, Familial Combined: DT, drug therapy

Lipoproteins, HDL: BL, blood

Lipoproteins, LDL Cholesterol: BL, blood

Lipoproteins, VLDL: BL, blood

Lovastatin: AD, administration & dosage

Lovastatin: AE, adverse effects

\*Lovastatin: TU, therapeutic use

Middle Age

Triglycerides: BL, blood

RN 41859-67-0 (Bezafibrate); 57-88-5 (Cholesterol); 75330-75-5 (Lovastatin)

CN 0 (Lipoproteins, HDL); 0 (Lipoproteins, LDL Cholesterol); 0 (Lipoproteins, VLDL); 0 (Triglycerides)

L173 ANSWER 13 OF 63 MEDLINE

AN 93110603 MEDLINE

DN 93110603 PubMed ID: 1471127

TI [Lovastatin in primary hypercholesterolemia. A Norwegian multicenter study].

Lovastatin ved primaer hyperkolesterolemi. En norsk multisenterstudie.

AU Ose L

CS Lipidklinikken, Rikshospitalet, Oslo.

SO TIDSSKRIFT FOR DEN NORSKE LAEGEFORENING, (1992 Nov 30) 112 (29) 3665-9.

Journal code: VRV; 0413423. ISSN: 0029-2001.

CY Norway

DT (CLINICAL TRIAL)

Journal; Article; (JOURNAL ARTICLE)

(MULTICENTER STUDY)

LA Norwegian

FS Priority Journals

EM 199301

ED Entered STN: 19930212

Last Updated on STN: 19930212

Entered Medline: 19930127

AB 266 patients with primary **hypercholesterolaemia** were followed for 48 weeks at 27 different centres to evaluate the safety, tolerability and effect on plasma lipids of **lovastatin** ranging from 20 to 80 mg/day. Mean change from baseline after 12 weeks of treatment with **lovastatin** was -34% (CI:33-35) for total **cholesterol**, -42% (CI:40-43) for LDL-**cholesterol**, +14% (CI:12-17) for HDL-**cholesterol** and -14% (CI:10-18) for triglycerides. Combination therapy with **cholestyramine** (8-24 g/day) was optional, and was started in 89 patients from week 13. At week 48 only 25% of all patients had obtained the second objective of the study: a total **cholesterol** value below 5.2 mmol/l. At the same time 60% of all patients had a total **cholesterol** below 6.2 mmol/l. Four patients dropped out of the study owing to adverse clinical experience. Only three of these events were probably related to **lovastatin**. Six patients were withdrawn because of adverse laboratory experiences. One patient showed clinical signs of myositis and increase of CK. In severe

primary **hypercholesterolaemia** combination therapy with **lovastatin** and a resin such as **cholestyramine** is required to obtain total **cholesterol** values below 5.2 mmol/l.

CT Check Tags: Female; Human; Male

Adult

Aged

**Cholesterol: BL, blood**

**\*Cholestyramine: AD, administration & dosage**

**Cholestyramine: AE, adverse effects**

Drug Evaluation

**Drug Therapy, Combination**

**Hypercholesterolemia: BL, blood**

**\*Hypercholesterolemia: DT, drug therapy**

**\*Lovastatin: AD, administration & dosage**

**Lovastatin: AE, adverse effects**

Middle Age

**Triglycerides: BL, blood**

RN **11041-12-6 (Cholestyramine); 57-88-5 (Cholesterol); 75330-75-5 (Lovastatin)**

CN **0 (Triglycerides)**

L173 ANSWER 14 OF 63 MEDLINE

AN 93096336 MEDLINE

DN 93096336 PubMed ID: 1461539

TI [Clinical evaluation of a selective inhibitor of **cholesterol** synthesis: pravastatin].

Valutazione clinica di un inibitore selettivo della sintesi del colesterolo: la pravastatina.

AU Alessandri C; Peverini F

CS Università degli Studi di Roma La Sapienza, Roma.

SO MINERVA MEDICA, (1992 Nov) 83 (11) 677-93. Ref: 98

Journal code: N6M; 0400732. ISSN: 0026-4806.

CY Italy

DT Journal; Article; (JOURNAL ARTICLE)

General Review; (REVIEW)

(REVIEW, TUTORIAL)

LA Italian

FS Priority Journals

EM 199301

ED Entered STN: 19930129

Last Updated on STN: 19980206

Entered Medline: 19930114

AB The recent introduction in clinical practice of a new class of drugs able to reduce the endogenous synthesis of **cholesterol** has undoubtedly made a noteworthy contribution to the treatment of **hypercholesterolaemia** which, as is well known, is one of the greatest risk factors in the natural history of atherosclerotic disease and of its cardiovascular complications. A last generation drug belonging to this family is pravastatin which differs from the other substances inhibiting the activity of the key enzyme of **cholesterol** metabolism, HMGCoA reductase, because of certain features of the molecule, such as hydrophilia and the fact it is already pharmacologically active at the moment of oral administration. Pravastatin, which is probably a special category of HMGCoA reductase inhibitor, has shown, in numerous experimental studies and controlled clinical trials, a notable effectiveness in reducing in a highly selective fashion the synthesis of **cholesterol** in the liver cells and consequently the number of **cholesterol**-rich lipoproteins in the systemic circulation, without also determining significant biologically negative side-effects.

CT Check Tags: Animal; Comparative Study; Female; Human; Male

Adult

**Anticholesteremic Agents: AD, administration & dosage**

**Anticholesteremic Agents: TU, therapeutic use**

**Cholesterol: BI, biosynthesis**

**Cholestyramine: TU, therapeutic use**

Clinical Trials

**Drug Therapy, Combination**

Guinea Pigs

Hydroxymethylglutaryl CoA Reductases: AI, antagonists &amp; inhibitors

\*Hypercholesterolemia: DT, drug therapy

Hypercholesterolemia: ET, etiology

Lovastatin: AA, analogs &amp; derivatives

Lovastatin: TU, therapeutic use

Pravastatin: AD, administration &amp; dosage

Pravastatin: AE, adverse effects

\*Pravastatin: TU, therapeutic use

Rats

Risk Factors

**Simvastatin**

Time Factors

RN 11041-12-6 (Cholestyramine); 57-88-5 (Cholesterol);  
75330-75-5 (Lovastatin); 79902-63-9 (Simvastatin); 81093-37-0  
(Pravastatin)

CN 0 (Anticholesteremic Agents); EC 1.1.1.88 (Hydroxymethylglutaryl  
CoA Reductases)

L173 ANSWER 15 OF 63 MEDLINE

AN 93031643 MEDLINE

DN 93031643 PubMed ID: 1412289

TI [Familial hypercholesterolemia--intensive diet therapy combined  
with drug therapy].

Familiaer hyperkolesterolemi--intensiv kostbehandling i kombinasjon med  
medikamentell behandling.

AU Stugaard M; Wiig I; Lund H; Ose L; Norseth J

CS Medisinsk avdeling A, Rikshospitalet, Oslo.

SO TIDSSKRIFT FOR DEN NORSKE LAEGEFORENING, (1992 Aug 30) 112 (20)  
2642-6.

Journal code: VRV; 0413423. ISSN: 0029-2001.

CY Norway

DT (CLINICAL TRIAL)

Journal; Article; (JOURNAL ARTICLE)

LA Norwegian

FS Priority Journals

EM 199211

ED Entered STN: 19930122

Last Updated on STN: 19930122

Entered Medline: 19921120

AB The aim of the investigation was twofold: to study the effect of  
**lovastatin**, a potent inhibitor of 3-hydroxy-3-methylglutaryl  
coenzyme A reductase, alone and in combination with other lipid lowering  
drugs in an open 48 week single centre study, and to study if lipid  
lowering drugs influence adherence to diet in adult patients with familial  
**hypercholesterolemia**. **Lovastatin** monotherapy (80 mg  
daily) for 12 weeks reduced serum **cholesterol**, **LDL-**  
**cholesterol** and triglycerides levels by 36%, 44% and 24%  
respectively. **HDL-cholesterol** level was increased by 12%. The  
addition of 16 g **cholestyramine** daily further increased the  
reduction of total **cholesterol** and **LDL-cholesterol**  
levels by 17% and 24% respectively. Addition of 1 g probucol daily  
decreased total **cholesterol**, **LDL-cholesterol** and **HDL-**  
**cholesterol** levels by 9%, 5% and 27% respectively. Addition of  
omega-3-fatty acids (3.6 g daily) reduced total **cholesterol**,  
**LDL-cholesterol** and triglycerides levels by 10%, 12% and 20%  
respectively. Administration of potent lipid lowering agents did not  
influence adherence to a diet with a mean daily fat energy of 21% (CI:  
20-22), **cholesterol** of 177 mg (CI: 157-196) and P/S ratio of  
0.75 (CI: 0.66-0.84). A significant increase in liver enzymes was recorded  
in only one patient. One patient was withdrawn from the study because of  
myositis.

CT Check Tags: Human

Adolescence

Adult

Aged

Antilipemic Agents: AE, adverse effects

\*Antilipemic Agents: TU, therapeutic use

Cholestyramine: AE, adverse effects

Cholestyramine: TU, therapeutic use

Drug Evaluation

Drug Therapy, Combination

Hypercholesterolemia, Familial: BL, blood

Hypercholesterolemia, Familial: DH, diet therapy

\*Hypercholesterolemia, Familial: DT, drug therapy

Lovastatin: AE, adverse effects

\*Lovastatin: TU, therapeutic use

Middle Age

RN 11041-12-6 (Cholestyramine); 75330-75-5 (Lovastatin)

CN 0 (Antilipemic Agents)

L173 ANSWER 16 OF 63 MEDLINE

AN 93024015 MEDLINE

DN 93024015 PubMed ID: 1406395

TI Successful management of primary hypercholesterolaemia with simvastatin and low-dose colestipol.

AU Simons L A; Simons J; Parfitt A

CS University of New South Wales, School of Medicine, Darlinghurst.

SO MEDICAL JOURNAL OF AUSTRALIA, (1992 Oct 5) 157 (7) 455-9.

Journal code: M26; 0400714. ISSN: 0025-729X.

CY Australia

DT (CLINICAL TRIAL)

Journal; Article; (JOURNAL ARTICLE)

(RANDOMIZED CONTROLLED TRIAL)

LA English

FS Priority Journals

EM 199210

ED Entered STN: 19930122

Last Updated on STN: 19980206

Entered Medline: 19921028

AB OBJECTIVE: To examine whether a small dose of bile acid sequestrant used in combination with a hydroxymethylglutaryl coenzyme A reductase inhibitor is more effective in reducing serum and low-density lipoprotein (LDL) **cholesterol** levels than inhibitor used alone. DESIGN: A randomised, double-blind study. SETTING: Subjects receiving tertiary care at a hospital lipid clinic. PATIENTS: Subjects with severe primary **hypercholesterolaemia** (types IIa and IIb), already stabilised on a **cholesterol**-lowering diet, with serum **cholesterol** levels of 7.0 mmol/L or more and triglyceride levels of 6.0 mmol/L or less. Sixty-four subjects were randomly assigned to the treatment groups; three withdrew before any outcome observations; 61 completed the trial and their results were analysed. INTERVENTIONS: Subjects were randomly assigned to receive either colestipol placebo or colestipol 5 g or 10 g each morning in fixed dosage for 18 weeks. They simultaneously received incremental doses of simvastatin: placebo for six weeks, then 20 mg/night for six weeks, then 40 mg/night for a final six weeks. MAIN OUTCOME MEASURES: Lipids, lipoproteins, and haematological and biochemical safety parameters were measured at the end of each treatment period. Adverse events were monitored. RESULTS: Respective maximum reductions (95% confidence intervals) in serum **cholesterol**, LDL **cholesterol** and apolipoprotein B (apo-B) values in subjects taking combination therapy were 41% (38%-45%), 50% (46%-53%) and 43% (39%-46%), compared with lesser reductions of 32% (26%-37%), 38% (31%-45%) and 37% (32%-41%) in those taking simvastatin monotherapy. The percentage changes in LDL **cholesterol** with combination therapy were independent of baseline **cholesterol** level or lipid phenotype. Combination therapy reduced serum triglyceride levels by up to 24% (15%-32%) and increased high-density lipoprotein (HDL) **cholesterol** levels by up to 9% (3%-15%). Three subjects withdrew within a few weeks because of severe gastrointestinal side effects related to colestipol; 19 experienced milder gastrointestinal side effects, 15 were taking combination therapy.

CONCLUSIONS: A combination of low-dose colestipol and simvastatin was found to be more effective in reducing serum and LDL **cholesterol** than simvastatin used alone. Such combination therapy offers the possibility of improved **cholesterol** lowering without the need for full dosage of either drug.

CT Check Tags: Human; Support, Non-U.S. Gov't

\***Anticholesteremic Agents: AD, administration & dosage**

**Anticholesteremic Agents: TU, therapeutic use**

Apolipoproteins B: BL, blood

**Cholesterol: BL, blood**

\***Colestipol: AD, administration & dosage**

**Colestipol: TU, therapeutic use**

Double-Blind Method

**Drug Therapy, Combination**

**Hypercholesterolemia: BL, blood**

\***Hypercholesterolemia: DT, drug therapy**

**Lipoproteins, HDL: BL, blood**

**Lipoproteins, LDL Cholesterol: BL, blood**

**Lovastatin: AD, administration & dosage**

\***Lovastatin: AA, analogs & derivatives**

**Lovastatin: TU, therapeutic use**

**Simvastatin**

Treatment Outcome

Triglycerides: BL, blood

RN 50925-79-6 (Colestipol); 57-88-5 (**Cholesterol**); 75330-75-5 (**Lovastatin**); 79902-63-9 (Simvastatin)

CN 0 (**Anticholesteremic Agents**); 0 (Apolipoproteins B); 0 (Lipoproteins, HDL); 0 (Lipoproteins, LDL **Cholesterol**); 0 (Triglycerides)

L173 ANSWER 17 OF 63 MEDLINE

AN 93005427 MEDLINE

DN 93005427 PubMed ID: 1392453

TI Long-term effect of **lovastatin** alone and in combination with **cholestyramine** on lipoprotein (a) level in familial **hypercholesterolemic** subjects.

AU Leren T P; Hjermann I; Foss O P; Leren P; Berg K

CS Department of Medical Genetics, Ullevaal Hospital, Oslo.

SO CLINICAL INVESTIGATOR, (1992 Aug) 70 (8) 711-8.

Journal code: BHE; 9207154. ISSN: 0941-0198.

CY GERMANY: Germany, Federal Republic of

DT Journal; Article; (JOURNAL ARTICLE)

LA English

FS Priority Journals

EM 199211

ED Entered STN: 19930122

Last Updated on STN: 19930122

Entered Medline: 19921117

AB We have determined the effect of **lovastatin** alone or in combination with **cholestyramine** on lipoprotein (a) [Lp(a)] levels in 59 heterozygotes for familial **hypercholesterolemia** (FH) treated for 33.8 (+/- 6.1) months. The median pretrial Lp(a) value was 10.2 mg/100 ml, which is twice the median value in healthy people examined at the Institute of Medical Genetics, University of Oslo. The median Lp(a) level was insignificantly reduced by 10.3% during the first 20 weeks when the subjects were on a standardized medication of increasing doses of **lovastatin** and **cholestyramine**. The first 20 weeks were followed by usual care treatment period, and a further decrease in Lp(a) level to 16.2% (P = 0.0012) was observed at the end of the study. Comparison between the 20 subjects on **lovastatin** monotherapy and the 31 subjects on the combined therapy of **lovastatin** and **cholestyramine**, revealed that the subjects on monotherapy had a median reduction of 20.1%, and the subjects on the combined therapy had a reduction of 15.4%. Thus, it appears that the reduction in Lp(a) level could be ascribed to **lovastatin** alone.

CT Check Tags: Female; Human; Male; Support, Non-U.S. Gov't



Adolescence

Adult

Aged

Apolipoproteins: BL, blood

\*Cholestyramine: AD, administration &amp; dosage

Cholestyramine: AE, adverse effects

Drug Therapy, Combination

Follow-Up Studies

Heterozygote

Hypercholesterolemia, Familial: BL, blood

\*Hypercholesterolemia, Familial: DT, drug therapy

Lipids: BL, blood

\*Lipoprotein(a): BL, blood

Lipoproteins: BL, blood

\*Lovastatin: AD, administration &amp; dosage

Lovastatin: AE, adverse effects

Middle Age

Time Factors

RN 11041-12-6 (Cholestyramine); 75330-75-5 (Lovastatin)

CN 0 (Apolipoproteins); 0 (Lipids); 0 (Lipoprotein(a)); 0 (Lipoproteins)

L173 ANSWER 18 OF 63 MEDLINE

AN 92387196 MEDLINE

DN 92387196 PubMed ID: 1516599

TI Short- and long-term effects of **lovastatin** and pravastatin alone  
and in combination with **cholestyramine** on serum lipids,  
lipoproteins and apolipoproteins in primary **hypercholesterolaemia**

AU Jacob B G; Mohrle W; Richter W O; Schwandt P

CS Department of Medicine II, University of Munich, FRG.

SO EUROPEAN JOURNAL OF CLINICAL PHARMACOLOGY, (1992) 42 (4) 353-8.

Journal code: EN4; 1256165. ISSN: 0031-6970.

CY GERMANY: Germany, Federal Republic of

DT Journal; Article; (JOURNAL ARTICLE)

LA English

FS Priority Journals

EM 199210

ED Entered STN: 19921023

Last Updated on STN: 19921023

Entered Medline: 19921006

AB The effects of the HMG CoA reductase inhibitors **lovastatin** and  
pravastatin on serum lipids, lipoproteins and apolipoproteins have been  
studied in 35 patients with primary **hypercholesterolaemia**. LDL  
**cholesterol** was lowered to the same extent by both agents compared  
on a mg basis of each drug per day. HDL **cholesterol** was  
increased by **lovastatin** but not by pravastatin. The reduction in  
serum triglycerides, VLDL triglycerides and VLDL **cholesterol** was  
more pronounced after **lovastatin** than pravastatin. After 1 year  
the effect of combined treatment with 40 mg pravastatin and 8 g  
**cholestyramine** on the reduction in LDL **cholesterol**  
(-39%) in 13 patients was comparable to that of 80 mg **lovastatin**  
plus 8 g **cholestyramine** (-40%) in 12 patients with identical  
baseline values. Differences were also found in the effects of the  
combination therapy with the two drugs on HDL **cholesterol**, serum  
triglycerides, VLDL triglycerides, VLDL **cholesterol**, and  
apolipoproteins.

CT Check Tags: Comparative Study; Female; Human; Male

Adolescence

Adult

Aged

Aged, 80 and over

\*Apolipoproteins: BL, blood

Apolipoproteins: DE, drug effects

Cholesterol: BL, blood

\*Cholestyramine: PD, pharmacology

Drug Therapy, Combination

**Hypercholesterolemia: BL, blood**

**\*Hypercholesterolemia: DT, drug therapy**

\*Lipids: BL, blood

\*Lipoproteins: BL, blood

Lipoproteins: DE, drug effects

**Lipoproteins, HDL Cholesterol: BL, blood**

**Lipoproteins, LDL Cholesterol: BL, blood**

**Lipoproteins, VLDL Cholesterol: BL, blood**

**\*Lovastatin: PD, pharmacology**

Middle Age

**\*Pravastatin: PD, pharmacology**

Time Factors

Triglycerides: BL, blood

RN **11041-12-6 (Cholestyramine); 57-88-5 (Cholesterol);**

**75330-75-5 (Lovastatin); 81093-37-0 (Pravastatin).**

CN 0 (Apolipoproteins); 0 (Lipids); 0 (Lipoproteins); 0 (Lipoproteins, HDL

**Cholesterol); 0 (Lipoproteins, LDL Cholesterol); 0**

**(Lipoproteins, VLDL Cholesterol); 0 (Triglycerides)**

L173 ANSWER 19 OF 63 MEDLINE

AN 92312488 MEDLINE

DN 92312488 PubMed ID: 1615846

TI Gemfibrozil-**lovastatin** therapy for primary hyperlipoproteinemias.

CM Comment in: Am J Cardiol. 1993 Feb 15;71(5):497

AU Glueck C J; Oakes N; Speirs J; Tracy T; Lang J

CS Cholesterol Center, Jewish Hospital, Cincinnati, Ohio 45229.

SO AMERICAN JOURNAL OF CARDIOLOGY, (1992 Jul 1) 70 (1) 1-9.

Journal code: 3DQ; 0207277. ISSN: 0002-9149.

CY United States

DT Journal; Article; (JOURNAL ARTICLE)

LA English

FS Abridged Index Medicus Journals; Priority Journals

EM 199207

ED Entered STN: 19920807

Last Updated on STN: 19920807

Entered Medline: 19920730

AB The specific aim of this retrospective, observational study was to assess safety and efficacy of long-term (21 months/patient), open-label, gemfibrozil-**lovastatin** treatment in 80 patients with primary mixed hyperlipidemia (68% of whom had atherosclerotic vascular disease). Because ideal lipid targets were not reached (low-density lipoprotein (LDL) **cholesterol** less than 130 mg/dl, high-density lipoprotein (HDL) **cholesterol** greater than 35 mg/dl, or total **cholesterol**/HDL **cholesterol** less than 4.5 mg/dl) with diet plus a single drug, gemfibrozil (1.2 g/day)-**lovastatin** (primarily 20 or 40 mg) treatment was given. Follow-up visits were scheduled with 2-drug therapy every 6 to 8 weeks, an average of 10.3 visits per patient, with 741 batteries of 6 liver function tests and 714 creatine phosphokinase levels measured. Only 1 of the 4,446 liver function tests (0.02%), a gamma glutamyl transferase, was greater than or equal to 3 times the upper normal limit. Of the 714 creatine phosphokinase levels, 9% were high; only 1 (0.1%) was greater than or equal to 3 times the upper normal limit. With 2-drug therapy, mean total **cholesterol** decreased 22% from 255 to 200 mg/dl, triglyceride levels decreased 35% from 236 to 154 mg/dl, LDL **cholesterol** decreased 26% from 176 to 131 mg/dl, and the total **cholesterol**/HDL **cholesterol** ratio decreased 24% from 7.1 to 5.4, all p less than or equal to 0.0001. Myositis, attributable to the drug combination and symptomatic enough to discontinue it, occurred in 3% of patients, and in 1% with concurrent high creatine phosphokinase (769 U/liter); no patients had rhabdomyolysis or myoglobinuria. (ABSTRACT TRUNCATED AT 250 WORDS)

CT Check Tags: Female; Human; Male; Support, Non-U.S. Gov't

Adult

Aged

Analysis of Variance

**Cholesterol: BL, blood**  
Combined Modality Therapy  
**Creatine Kinase: BL, blood**  
**Drug Therapy, Combination**  
Gemfibrozil: AE, adverse effects  
\*Gemfibrozil: TU, therapeutic use  
**Hyperlipoproteinemia: BL, blood**  
**Hyperlipoproteinemia: DH, diet therapy**  
\***Hyperlipoproteinemia: DT, drug therapy**  
Liver Function Tests  
**Lovastatin: AE, adverse effects**  
\***Lovastatin: TU, therapeutic use**  
Middle Age  
Myositis: CI, chemically induced  
Retrospective Studies  
Triglycerides: BL, blood

RN 25812-30-0 (Gemfibrozil); 57-88-5 (**Cholesterol**); 75330-75-5  
(**Lovastatin**)  
CN 0 (Triglycerides); EC 2.7.3.2 (Creatine Kinase)

L173 ANSWER 20 OF 63 MEDLINE

AN 92275541 MEDLINE

DN 92275541 PubMed ID: 1592346

TI Effect of simvastatin, ursodeoxycholic acid and simvastatin plus  
ursodeoxycholic acid on biliary lipid secretion and cholic acid kinetics  
in nonfamilial **hypercholesterolemia**.

AU Mazzella G; Parini P; Festi D; Bazzoli F; Aldini R; Roda A; Tonelli D;  
Cipolla A; Salzetta A; Roda E

CS Cattedra di Gastroenterologia, University of Bologna, Italy.

SO HEPATOLOGY, (1992 Jun) 15 (6) 1072-8.

Journal code: GBZ; 8302946. ISSN: 0270-9139.

CY United States

DT (CLINICAL TRIAL)

Journal; Article; (JOURNAL ARTICLE)

(RANDOMIZED CONTROLLED TRIAL)

LA English

FS Priority Journals

EM 199206

ED Entered STN: 19920710

Last Updated on STN: 19990129

Entered Medline: 19920626

AB It has been recently shown that the newest **hypocholesterolemic**  
agent, simvastatin, lowers the biliary **cholesterol** saturation  
index and that its association with ursodeoxycholic acid renders it more  
effective. To determine the mechanism by which simvastatin decreases the  
biliary **cholesterol** saturation index, we evaluated hepatic  
secretion rates of **cholesterol**, bile acids and phospholipids,  
and cholic acid pool size, turnover and synthesis in eight hyperlipidemic  
patients (five women and three men, age range = 38 to 65 yr). These  
assessments were conducted before treatment, after 4 wk of simvastatin (40  
mg/day), after 4 wk of ursodeoxycholic acid (600 mg/day) and after a  
further 4 wk of a combination therapy of simvastatin (40 mg/day) plus  
ursodeoxycholic acid (600 mg/day). The **cholesterol** saturation  
index was significantly reduced with simvastatin (from 1.51 +/- 0.10 to  
0.94 +/- 0.05, mean +/- S.E.; p less than 0.02), with ursodeoxycholic acid  
(from 1.51 +/- 0.10 to 0.86 +/- 0.03, mean +/- S.E.; p less than 0.02) and  
with the combination of simvastatin plus ursodeoxycholic acid (from 1.51  
+/- 0.01 to 0.70 +/- 0.05, p less than 0.02). The **cholesterol**  
saturation index during combination therapy was significantly lower (p  
less than 0.02) than that reached during the use of simvastatin and  
ursodeoxycholic acid. Both simvastatin and ursodeoxycholic acid  
significantly reduced the hepatic secretion rate of **cholesterol**  
(from 130 +/- 14 mumols/hr to 81 +/- 12 mumols/hr, p less than 0.01, and  
70 +/- 9 mumols/hr, p less than 0.01) without affecting bile acid and  
phospholipid outputs. (ABSTRACT TRUNCATED AT 250 WORDS)

CT Check Tags: Female; Human; Male

Adult

Aged

\*Anticholesteremic Agents: TU, therapeutic use

\*Bile: ME, metabolism

Cholesterol: ME, metabolism

Cholic Acid

Cholic Acids: BI, biosynthesis

\*Cholic Acids: ME, metabolism

Drug Therapy, Combination

Hydroxymethylglutaryl CoA Reductases: AI, antagonists & inhibitors

\*Hypercholesterolemia: DT, drug therapy

Hypercholesterolemia: ME, metabolism

Kinetics

\*Lipids: ME, metabolism

Liver: ME, metabolism

\*Lovastatin: AA, analogs & derivatives

Lovastatin: TU, therapeutic use

Middle Age

Simvastatin

\*Ursodeoxycholic Acid: TU, therapeutic use

RN 128-13-2 (Ursodeoxycholic Acid); 57-88-5 (Cholesterol);  
75330-75-5 (Lovastatin); 79902-63-9 (Simvastatin); 81-25-4 (Cholic  
Acid)

CN 0 (Anticholesteremic Agents); 0 (Cholic Acids); 0 (Lipids); EC  
1.1.1.88 (Hydroxymethylglutaryl CoA Reductases)

L173 ANSWER 21 OF 63 MEDLINE

AN 92247097 MEDLINE

DN 92247097 PubMed ID: 1811555

TI Response to **cholesterol**-lowering drugs in familial defective  
apolipoprotein B-100.

AU Maher V M; Gallagher J J; Thompson G R; Myant N B

CS MRC Lipoprotein Team, Hammersmith Hospital, London, U.K.

SO ATHEROSCLEROSIS, (1991 Nov) 91 (1-2) 73-6.

Journal code: 95X; 0242543. ISSN: 0021-9150.

CY Netherlands

DT Journal; Article; (JOURNAL ARTICLE)

LA English

FS Priority Journals

EM 199206

ED Entered STN: 19920619

Last Updated on STN: 19980206

Entered Medline: 19920603

AB The effect of **cholestyramine** and simvastatin, given separately  
or in combination, on serum lipid concentrations in 11 patients with  
heterozygous familial defective apolipoprotein B-100 was compared with  
that in 11 matched patients with heterozygous familial  
**hypercholesterolaemia**. In both groups of patients there was a  
substantial fall in serum lipid levels in response to treatment. There  
were no significant differences between the reductions in serum total or  
low-density lipoprotein **cholesterol** levels in the two groups.

CT Check Tags: Comparative Study; Female; Human; Male; Support, Non-U.S.  
Gov't

Adult

Aged

\*Anticholesteremic Agents: TU, therapeutic use

\*Apolipoproteins B: GE, genetics

Apolipoproteins E: GE, genetics

Cholesterol: BL, blood

Cholestyramine: TU, therapeutic use

Drug Therapy, Combination

Heterozygote

Hypercholesterolemia: BL, blood

\*Hypercholesterolemia: DT, drug therapy

Hypercholesterolemia: GE, genetics

Lipoproteins, LDL Cholesterol: BL, blood

**Lovastatin: AA, analogs & derivatives**

**Lovastatin: TU, therapeutic use**

Middle Age

Phenotype

**Simvastatin**

Triglycerides: BL, blood

RN 11041-12-6 (**Cholestyramine**); 57-88-5 (**Cholesterol**);

75330-75-5 (**Lovastatin**); 79902-63-9 (**Simvastatin**)

CN 0 (**Anticholesteremic Agents**); 0 (**Apolipoproteins B**); 0  
(**Apolipoproteins E**); 0 (**Lipoproteins, LDL Cholesterol**); 0  
(**Triglycerides**); 0 (**apolipoprotein B-100**)

L173 ANSWER 22 OF 63 MEDLINE

AN 92177766 MEDLINE

DN 92177766 PubMed ID: 1724525

TI Combination therapy with **lovastatin** and guar gum versus  
**lovastatin** and **cholestyramine** in treatment of  
**hypercholesterolemia**.

AU Uusitupa M; Ebeling T; Happonen P; Voutilainen E; Turtola H; Parviainen M;  
Pyorala K

CS Department of Medicine, University of Kuopio, Finland.

SO JOURNAL OF CARDIOVASCULAR PHARMACOLOGY, (1991 Oct) 18 (4)  
496-503.

Journal code: K78; 7902492. ISSN: 0160-2446.

CY United States

DT (CLINICAL TRIAL)

Journal; Article; (JOURNAL ARTICLE)

(RANDOMIZED CONTROLLED TRIAL)

LA English

FS Priority Journals

EM 199204

ED Entered STN: 19920424

Last Updated on STN: 19960129

Entered Medline: 19920407

AB Sixty-two patients (34 men and 28 women) aged 19-64 years, half of whom  
had familial **hypercholesterolemia**, treated initially for 18  
weeks with **lovastatin** alone were randomly allocated either to  
**lovastatin** (L) and **cholestyramine** (16 g/day) or  
**lovastatin** and guar gum (L + GG 20 g/day) treatment for 18  
additional weeks to compare the **hypocholesterolemic** effects of  
these two combination therapies. The patients were selected for this study  
from a larger study of patients (n = 120) with severe  
**hypercholesterolemia** [serum total **cholesterol** (serum  
Chol) 6.5-16.3 mM before treatment], and only those patients in whom serum  
Chol after **lovastatin** alone (dose 80 mg/day) remained greater  
than or equal to 5.2 mM were eligible for evaluation of combination  
therapies. Serum Chol decreased from 10.6 +/- 1.6 to 5.9 +/- 1.3 mM (mean  
+/- SD) (p less than 0.001) and low-density lipoprotein  
**cholesterol** (LDL Chol) from 8.5 +/- 1.8 to 4.1 +/- 1 mM (p less  
than 0.001) in patients treated with L + GG (values before the beginning  
of **lovastatin** and at the end of the combination therapy). The  
respective changes were from 10.9 +/- 2.2 to 5.5 +/- 1.2 mM (p less than  
0.001) and from 8.7 +/- 2.3 to 3.5 +/- 1.2 mM (p less than 0.001) in  
patients treated with **lovastatin** and **cholestyramine** (L  
+ C). At the end of the study, both serum Chol (p less than 0.005) and LDL  
Chol (p less than 0.01) were significantly lower with L + C than with L +  
GG. (ABSTRACT TRUNCATED AT 250 WORDS)

CT Check Tags: Comparative Study; Female; Human; Male; Support, Non-U.S.  
Gov't

Adult

Aged

Apolipoprotein A-I: ME, metabolism

Apolipoproteins B: ME, metabolism

Blood Pressure: DE, drug effects

Body Weight: DE, drug effects

**Cholestyramine: AD, administration & dosage**

**Cholestyramine: AE, adverse effects**  
**\*Cholestyramine: TU, therapeutic use**  
 Double-Blind Method  
 Drug Therapy, Combination  
 Galactans: AD, administration & dosage  
 Galactans: AE, adverse effects  
**\*Galactans: TU, therapeutic use**  
 Hypercholesterolemia: BL, blood  
**\*Hypercholesterolemia: DT, drug therapy**  
 Hypercholesterolemia, Familial: BL, blood  
 Hypercholesterolemia, Familial: DT, drug therapy  
 Lipids: BL, blood  
 Lovastatin: AD, administration & dosage  
 Lovastatin: AE, adverse effects  
**\*Lovastatin: TU, therapeutic use**  
 Mannans: AD, administration & dosage  
 Mannans: AE, adverse effects  
**\*Mannans: TU, therapeutic use**

Middle Age

RN 11041-12-6 (Cholestyramine); 75330-75-5 (Lovastatin);  
 9000-30-0 (guar gum)  
 CN 0 (Apolipoprotein A-I); 0 (Apolipoproteins B); 0 (Galactans); 0 (Lipids);  
 0 (Mannans)

L173 ANSWER 23 OF 63 MEDLINE

AN 92162100 MEDLINE

DN 92162100 PubMed ID: 1789813

TI Long-term efficacy and safety of simvastatin alone and in combination therapy in treatment of **hypercholesterolaemia**.

AU Molgaard J; Lundh B L; von Schenck H; Olsson A G

CS Department of Internal Medicine, Faculty of Health Sciences, University Hospital, Linköping, Sweden.

SO ATHEROSCLEROSIS, (1991 Dec) 91 Suppl S21-8.

Journal code: 95X; 0242543. ISSN: 0021-9150.

CY Netherlands

DT (CLINICAL TRIAL)

(CONTROLLED CLINICAL TRIAL)

Journal; Article; (JOURNAL ARTICLE)

LA English

FS Priority Journals

EM 199203

ED Entered STN: 19920410

Last Updated on STN: 19980206

Entered Medline: 19920325

AB The 3-years efficacy and safety of the 3-hydroxy-3-methylglutaryl coenzyme A reductase inhibitor simvastatin (S) (previously called synvinolin or MK-733) has been studied in single and combined therapy with **cholestyramine** (C) in 48 **hypercholesterolaemic** patients.

Plasma lipids, lipoproteins and apolipoproteins A-I and B, and blood safety tests (haematology, liver function, creatine phosphokinase (CPK), creatinine, blood glucose and thyroid function) were determined regularly throughout the study. Extensive ophthalmological examinations with particular focus on the lens were done before initiation of therapy and at every 6 months during drug treatment. Maximal reductions of mean plasma total **cholesterol** concentration (34% with S; 47% with S + C) and low-density lipoprotein (LDL)-**cholesterol** concentration (42% with S; 56% with S + C) were achieved after 4 weeks on full-dose therapy. During continued treatment, years 1 through 3, the reduction of mean plasma total **cholesterol** was 26-29% with S alone, and 31-41% with S + C. Significant reductions of plasma triglycerides (15-27%) and very low density lipoprotein (VLDL) triglycerides (10-27%) were achieved in the group treated with S as single therapy. In this group there was also a significant increase (10-14%) of high-density lipoprotein (HDL)-**cholesterol**. In liver aspartate (AST) and alanine (ALT) aminotransferases, as well as alkaline phosphatase (ALP), minor and variable, but usually transient, increases were seen. Repeated

ophthalmological examinations did not demonstrate any drug-related side effects. It is concluded that simvastatin is a safe and efficient **cholesterol**-lowering drug for long-term therapy, both as a single drug and in combination with **cholestyramine**.

CT Check Tags: Female; Human; Male; Support, Non-U.S. Gov't

Adult

Aged

\*Anticholesteremic Agents: AD, administration & dosage

Anticholesteremic Agents: AE, adverse effects

Cholestyramine: TU, therapeutic use

Clinical Trials

Drug Therapy, Combination

\*Hydroxymethylglutaryl CoA Reductases: AI, antagonists & inhibitors

Hypercholesterolemia: BL, blood

\*Hypercholesterolemia: DT, drug therapy

Lens, Crystalline: DE, drug effects

Lipids: BL, blood

Liver: DE, drug effects

Lovastatin: AD, administration & dosage

Lovastatin: AE, adverse effects

\*Lovastatin: AA, analogs & derivatives

Middle Age

Simvastatin

RN 11041-12-6 (Cholestyramine); 75330-75-5 (Lovastatin);

79902-63-9 (Simvastatin)

CN 0 (Anticholesteremic Agents); 0 (Lipids); EC 1.1.1.88

(Hydroxymethylglutaryl CoA Reductases)

L173 ANSWER 24 OF 63 MEDLINE

AN 92152564 MEDLINE

DN 92152564 PubMed ID: 1785747

TI [Study of LDL receptors and response to **lovastatin** therapy in familial homozygotic **hypercholesterolemia**].

Estudio de receptores del colesterol LDL y respuesta del tratamiento con **lovastatina** en la hipercolesterolemia familiar homocigota.

AU Ausina Gomez A; Gilsanz Peral A; Montero Brens C; Dalmau Serra J

CS Unidad de Nutricion, Hospital Infantil La Fe, Valencia.

SO ANALES ESPANOLAS DE PEDIATRIA, (1991 Nov) 35 (5) 327-31. Ref: 18

Journal code: 49N; 0420463. ISSN: 0302-4342.

CY Spain

DT Journal; Article; (JOURNAL ARTICLE)

General Review; (REVIEW)

(REVIEW, TUTORIAL)

LA Spanish

FS Priority Journals

EM 199203

ED Entered STN: 19920405

Last Updated on STN: 19920405

Entered Medline: 19920319

AB This study shows the results obtained with **lovastatin** as a combined therapy with probucol and **cholestyramine** on the lipid profile of two patients with homozygous familial **hypercholesterolemia**. Both have been diagnosed according to the clinical and biochemical criteria (type IIa **hypercholesterolemia**) as well as by the **cholesterol** or low density lipoprotein (LDL-C) receptor analysis. After the initial probucol and **cholestyramine** treatment we observed a drop of total **cholesterol** (T-C) of 41.7% and 46% as well as LDL-C of 51.6% and 49.3% in both patients. Respectively when **lovastatin** were associated an additional drop of T-C of 23.7%, LDL-C of 23.2%, high-density lipoprotein **cholesterol** (HDL-C) of 22.4% and the apoprotein B (Apo B) of 37% were obtained in one patient (receptor-defective) but no change in the lipid profile were obtained in the other patient (receptor-negative). No adverse effects were observed with this drug. This drug could be of help as a combined therapy in the

treatment of homozygous familial **hypercholesterolemia**, even though the treatment of choice is the LDL-plasma feresis and/or liver transplantation. We expound the difficulties relate to LDL receptor study in homocygous receptor-negative patients.

CT Check Tags: Human

**Cholestyramine: TU, therapeutic use**

**Drug Therapy, Combination**

Homozygote

**\*Hypercholesterolemia, Familial: DT, drug therapy**

**Hypercholesterolemia, Familial: GE, genetics**

**\*Lovastatin: TU, therapeutic use**

**\*Receptors, LDL: DE, drug effects**

RN 11041-12-6 (Cholestyramine); 75330-75-5 (Lovastatin)

CN 0 (Receptors, LDL)

L173 ANSWER 25 OF 63 MEDLINE

AN 92017348 MEDLINE

DN 92017348 PubMed ID: 1921811

TI Treatment of primary **hypercholesterolaemia** with simvastatin. New Zealand multicentre evaluation.

AU Lintott C J; Scott R S; Sharpe D N; Nye E R; Charleson H; French J K; White H D; Reuben S; Maling T J; Lewis G R; +

CS Princess Margaret Hospital, Christchurch, New Zealand.

SO MEDICAL JOURNAL OF AUSTRALIA, (1991 Oct 7) 155 (7) 433-6.

Journal code: M26; 0400714. ISSN: 0025-729X.

CY Australia

DT (CLINICAL TRIAL)

Journal; Article; (JOURNAL ARTICLE)

(MULTICENTER STUDY)

LA English

FS Priority Journals

EM 199111

ED Entered STN: 19920124

Last Updated on STN: 19980206

Entered Medline: 19911107

AB OBJECTIVE: To assess the efficacy of simvastatin in a large patient cohort. DESIGN: In an open multicentre study, after a four week placebo phase, patients were treated with simvastatin for 24 weeks; a subgroup continued therapy for a further 24 weeks. Efficacy of simvastatin (a) with prolonged use over three years, and (b) in combination with bezafibrate was assessed in an open single site study. SETTING: Lipid or cardiology specialist hospital outpatient clinics. PATIENTS: For the open multicentre study, 228 patients with primary **hypercholesterolaemia** (total **cholesterol** level greater than 6.5 mmol/L) were recruited, of whom 224 met entry criteria and completed the study. Forty-seven of these patients continued therapy for one year. In the open single site study, 22 patients (with low density lipoprotein [LDL] **cholesterol** levels greater than 4.3 mmol/L) participated in studies of long term use (n = 9) or of combined therapy (n = 13). INTERVENTION: Therapy in the open multicentre study began with 10 mg of simvastatin per day, doubling to 20 mg after six weeks and then 40 mg after 12 weeks of therapy if total **cholesterol** levels persisted above 5.2 mmol/L. In the study of long term use, simvastatin (40 mg daily) was taken continuously over three years. In the study of combination therapy, bezafibrate (600 mg daily) was taken in addition to simvastatin (40 mg daily) for 10 months. MAIN OUTCOME MEASURES: Plasma lipid and lipoprotein concentrations. RESULTS: In the multicentre study, total plasma **cholesterol** levels were reduced by 32.8% from 9.11 +/- 1.84 (in mmol/L, mean +/- SD) to 6.12 +/- 1.25 (P less than 0.001), and LDL **cholesterol** levels by 41.4% from 6.90 +/- 1.92 to 4.04 +/- 0.31 (P less than 0.001). The effect of therapy was sustained in those patients continuing therapy to 48 weeks. The study of long term use found no significant attenuation of effect over three years of monotherapy. Combined simvastatin/bezafibrate therapy reduced the LDL **cholesterol** concentration by a further 19.9% (P less than 0.001) from levels achieved on simvastatin alone. CONCLUSIONS: Simvastatin is an effective, well tolerated lipid lowering drug, without significant



attenuation of effect with prolonged use. Simvastatin plus bezafibrate appears to be a potentially useful drug combination.

CT Check Tags: Female; Human; Male

Adult

Aged

Anticholesteremic Agents: AE, adverse effects

\*Anticholesteremic Agents: TU, therapeutic use

Bezafibrate: TU, therapeutic use

Cholesterol: BL, blood

Cohort Studies

Drug Therapy, Combination

Hypercholesterolemia: BL, blood

\*Hypercholesterolemia: DT, drug therapy

Lipoproteins, LDL Cholesterol: BL, blood

Lovastatin: AE, adverse effects

\*Lovastatin: AA, analogs & derivatives

Lovastatin: TU, therapeutic use

Middle Age

New Zealand

Simvastatin

RN 41859-67-0 (Bezafibrate); 57-88-5 (Cholesterol); 75330-75-5 (Lovastatin); 79902-63-9 (Simvastatin)

CN 0 (Anticholesteremic Agents); 0 (Lipoproteins, LDL Cholesterol)

L173 ANSWER 26 OF 63 MEDLINE

AN 91349303 MEDLINE

DN 91349303 PubMed ID: 1880219

TI Lecithin: **cholesterol** acyltransferase activity in familial **hypercholesterolemia** treated with simvastatin and simvastatin plus low-dose colestipol.

AU Desager J P; Horsmans Y; Harvengt C

CS Laboratoire de Pharmacotherapie, Universite Catholique de Louvain, Brussels, Belgium.

SO JOURNAL OF CLINICAL PHARMACOLOGY, (1991 Jun) 31 (6) 537-42.

Journal code: HT9; 0366372. ISSN: 0091-2700.

CY United States

DT Journal; Article; (JOURNAL ARTICLE)

LA English

FS Priority Journals

EM 199110

ED Entered STN: 19911020

Last Updated on STN: 19980206

Entered Medline: 19911003

AB In 19 patients with heterozygous familial **hypercholesterolemia** (FH), the effects of simvastatin (S) 20 mg/d, 40 mg/d, and 40 mg/d plus low-dose colestipol (10 g/d) on plasma lipids, plasma lipoproteins, and plasma lecithin: **cholesterol** acyltransferase (LCAT) activity were investigated after an original dose-range escalation/descalation design. The drug regimen was changed every 8 weeks. A significant reduction in total **cholesterol** and LDL-**cholesterol** was observed, reaching 39% and 54% for the drug combination (week 28), and total apoprotein B and LDL-apoprotein B were reduced by 39% and 50%, respectively. Triglycerides were significantly lowered by S alone (up to 29% with 40 mg/d). HDL-**cholesterol** increased during therapy but the **cholesterol** content in HDL2-HDL3 fractions (isolated by ultracentrifugation) did not change significantly during the different steps. The ratio LDL-C/HDL-C fell by 57% at week 28. Plasma LCAT activity expressed as FER was significantly enhanced by S alone (+33%), and a further increase on drug combination regimen (+58%) was observed. This effect could be considered as a consequence of the increased fractional clearance of LDL-C. It tended to be sustained during the descalation part of the study. Biochemical adverse effects were scarce and transient. In conclusion, the combination therapy increased the plasma LCAT/FER activity without a preferential enhancement in HDL2-C concentration. This original design allowed to define the most appropriate individual

**cholesterol**-lowering drug dosage in FH patients.

CT Check Tags: Comparative Study; Female; Human; Male; Support, Non-U.S. Gov't  
 Adolescence  
 Adult  
**Anticholesteremic Agents: AD, administration & dosage**  
**\*Anticholesteremic Agents: TU, therapeutic use**  
 Colestipol: AD, administration & dosage  
**\*Colestipol: TU, therapeutic use**  
**Drug Therapy, Combination**  
**\*Hypercholesterolemia, Familial: BL, blood**  
**Hypercholesterolemia, Familial: DT, drug therapy**  
**Hypercholesterolemia, Familial: EN, enzymology**  
**Lovastatin: AD, administration & dosage**  
**\*Lovastatin: AA, analogs & derivatives**  
**Lovastatin: TU, therapeutic use**  
 Middle Age  
**\*Phosphatidylcholine-Sterol O-Acyltransferase: BL, blood**  
 Phosphatidylcholine-Sterol O-Acyltransferase: ME, metabolism  
**Simvastatin**

RN 50925-79-6 (Colestipol); **75330-75-5 (Lovastatin)**; 79902-63-9 (Simvastatin)

CN 0 (**Anticholesteremic Agents**); EC 2.3.1.43 (Phosphatidylcholine-Sterol O-Acyltransferase)

L173 ANSWER 27 OF 63 MEDLINE

AN 91262174 MEDLINE

DN 91262174 PubMed ID: 2047557

TI [Treatment of **hypercholesterolemic** patients of different age with simvastatin: 1-year study].  
 Trattamento di pazienti ipercolesterolemici di diversa eta con simvastatina. Studio di un anno.

AU Pernigotti L; Bo M; Poli L; Zancocchi M; Fiandra U; Pedrazzini V; Fabris F

CS Istituto di Medicina e Chirurgia geriatrica, Ospedale Molinette, Universita, Torino.

SO RECENTI PROGRESSI IN MEDICINA, (1991 Mar) 82 (3) 155-62.  
 Journal code: R1T; 0401271. ISSN: 0034-1193.

CY Italy

DT (CLINICAL TRIAL)  
 Journal; Article; (JOURNAL ARTICLE)

LA Italian

FS Priority Journals

EM 199107

ED Entered STN: 19910802  
 Last Updated on STN: 19980206  
 Entered Medline: 19910718

AB Nowadays there is no direct evidence that lowering **cholesterol** may reduce the CHD in the elderly; however, several evidences suggest the potential benefit of a dietetic and/or pharmacologic intervention in healthy young-old **hypercholesterolemics**. In this study we evaluated the efficacy and tolerability of simvastatin, alone or in combination with **cholestyramine**, in two groups of patients (group A: age 30-55 years and group B: age 60-75 years) with primary **hypercholesterolemia**, over a 48-week period. In both groups Simvastatin induced a significant reduction in total and LDL **cholesterol** (p less than 0.001 both), with a decrease of the total/HDL **cholesterol** ratio (p less than 0.001). A reduction of the apo-B100 levels was also observed (respectively p less than 0.01 and p less than 0.001) with a significant improvement of the apo-B100/apo-A1 ratio (p less than 0.01). Simvastatin was well tolerated and free of remarkable side effects in both groups.

CT Check Tags: Comparative Study; Human  
 Adult  
 Age Factors  
 Aged  
**Anticholesteremic Agents: AD, administration & dosage**

\*Anticholesteremic Agents: TU, therapeutic use  
   Cholesterol: BL, blood  
   Cholestyramine: AD, administration & dosage  
   Drug Therapy, Combination  
 \*Hydroxymethylglutaryl CoA Reductases: AI, antagonists & inhibitors  
   Hypercholesterolemia: BL, blood  
   \*Hypercholesterolemia: DT, drug therapy  
   Lipoproteins, LDL Cholesterol: BL, blood  
   Lovastatin: AD, administration & dosage  
   \*Lovastatin: AA, analogs & derivatives  
   Lovastatin: TU, therapeutic use  
   Middle Age  
   Simvastatin  
   Time Factors  
 RN 11041-12-6 (Cholestyramine); 57-88-5 (Cholesterol);  
   75330-75-5 (Lovastatin); 79902-63-9 (Simvastatin)  
 CN 0 (Anticholesteremic Agents); 0 (Lipoproteins, LDL  
   Cholesterol); EC 1.1.1.88 (Hydroxymethylglutaryl CoA Reductases)

L173 ANSWER 28 OF 63 MEDLINE  
 AN 91160023 MEDLINE  
 DN 91160023 PubMed ID: 2073670  
 TI Combination drug therapy with HMG CoA reductase inhibitors and bile acid  
   sequestrants for hypercholesterolemia.  
 AU Erkelens D W  
 CS University Hospital, Utrecht, The Netherlands.  
 SO CARDIOLOGY, (1990) 77 Suppl 4 33-8.  
   Journal code: COI; 1266406. ISSN: 0008-6312.  
 CY Switzerland  
 DT Journal; Article; (JOURNAL ARTICLE)  
 LA English  
 FS Priority Journals  
 EM 199104  
 ED Entered STN: 19910505  
   Last Updated on STN: 19980206  
   Entered Medline: 19910416  
 AB Single-drug therapy is often not sufficient to lower total and low-density  
   lipoprotein (LDL) **cholesterol** levels in patients with familial  
   **hypercholesterolemia** to desirable or target levels. Therefore,  
   combination drug therapy is often necessary. The most potent therapy to  
   achieve this goal is a combination of a 3-hydroxy-3-methylglutaryl  
   coenzyme A (HMG CoA) reductase inhibitor, which reduces  
   **cholesterol** synthesis, and a bile acid sequestrant, which  
   indirectly depletes the intrahepatic **cholesterol** pool. LDL  
   **cholesterol** reductions reportedly vary between 52 and 54% in  
   short-term trials. Combining a bile acid sequestrant with nicotinic acid  
   reduces LDL **cholesterol** 34-55%, and with a fibrate, 12-42%. The  
   triple-drug regimen of bile acid sequestrant, an HMG CoA reductase  
   inhibitor, and nicotinic acid is even more effective, achieving reductions  
   of 59-67%. All these regimens elevate high-density lipoprotein  
   **cholesterol** levels concomitantly by 2-37%.  
 CT Check Tags: Human  
   \*Cholestyramine: AD, administration & dosage  
   Cholestyramine: TU, therapeutic use  
   Drug Therapy, Combination  
   Hydroxymethylglutaryl CoA Reductases: AD, administration & dosage  
   \*Hydroxymethylglutaryl CoA Reductases: AI, antagonists & inhibitors  
   Hypercholesterolemia, Familial: BL, blood  
   \*Hypercholesterolemia, Familial: DT, drug therapy  
   Lipids: BL, blood  
   Lovastatin: AD, administration & dosage  
   Lovastatin: AA, analogs & derivatives  
   Lovastatin: TU, therapeutic use  
   Niacin: AD, administration & dosage  
   Niacin: TU, therapeutic use  
   Simvastatin

RN 11041-12-6 (**Cholestyramine**); 59-67-6 (Niacin); 75330-75-5  
(**Lovastatin**); 79902-63-9 (Simvastatin)  
CN 0 (Lipids); EC 1.1.1.88 (Hydroxymethylglutaryl CoA Reductases)

L173 ANSWER 29 OF 63 MEDLINE

AN 91138290 MEDLINE

DN 91138290 PubMed ID: 2149540

TI [The treatment of refractory hyperlipoproteinemias].

Il trattamento delle iperlipoproteinemie resistenti.

AU Barone A; Ansuini R; Francolini G; Frausini G; Pupita F

CS Divisione di Medicina Interna, Ospedale Unificato di Fano-Mondolfo.

SO CLINICA TERAPEUTICA, (1990 Oct 15) 135 (1) 31-6.

Journal code: DKN; 0372604. ISSN: 0009-9074.

CY Italy

DT Journal; Article; (JOURNAL ARTICLE)

LA Italian

FS Priority Journals

EM 199103

ED Entered STN: 19910412

Last Updated on STN: 19980206

Entered Medline: 19910327

AB The authors have studied a group of 25 patients treated with an HMG-CoA reductase inhibitor associated with DEAE-dextran, a safe and useful drug for the treatment of dyslipidemia. The patients were selected from a group of subjects previously submitted to long-term treatment with an HMG-CoA reductase inhibitor only who had failed to achieve normal **cholesterol** blood levels. The combined treatment with DEAE-dextran (1.5 g 3 times daily) and simvastatin (20 mg once daily) for 90 days lead to a further significant decrease in **cholesterol** and triglyceride blood levels. These findings confirm the validity of the association of an ion exchange resin with an HMG-CoA reductase inhibitor in the treatment of refractory dyslipidemias.

CT Check Tags: Female; Human; Male

**Anticholesteremic Agents: TU, therapeutic use**

**Cholesterol: BL, blood**

**DEAE-Dextran: TU, therapeutic use**

Drug Evaluation

**Drug Therapy, Combination**

**Hyperlipoproteinemia: BL, blood**

**\*Hyperlipoproteinemia: DT, drug therapy**

**Lovastatin: AA, analogs & derivatives**

**Lovastatin: TU, therapeutic use**

Middle Age

**Simvastatin**

Triglycerides: BL, blood

RN 57-88-5 (**Cholesterol**); 75330-75-5 (**Lovastatin**);

79902-63-9 (Simvastatin); 9015-73-0 (DEAE-Dextran)

CN 0 (**Anticholesteremic Agents**); 0 (Triglycerides)

L173 ANSWER 30 OF 63 MEDLINE

AN 91069076 MEDLINE

DN 91069076 PubMed ID: 2252289

TI [Homozygous familial **hypercholesterolemia**. Response to combined

**cholestyramine** and **lovastatin** therapy].

Hipercolesterolemia familiar homocigota. Respuesta al tratamiento combinado con colestiramina y **lovastatina**.

AU Obando Santaella I; Fernandez Gomez E; Mongil Ruiz I; Escobar Gallego A;

Garcia Alegria J J; Gascon Luna F; Masana Marin L

CS Servicio de Pediatria, Hospital G B de Pozoblanco, Cordoba.

SO ANALES ESPANOLAS DE PEDIATRIA, (1990 Jul) 33 (1) 58-60.

Journal code: 49N; 0420463. ISSN: 0302-4342.

CY Spain

DT Journal; Article; (JOURNAL ARTICLE)

LA Spanish

FS Priority Journals

EM 199101

ED Entered STN: 19910308  
Last Updated on STN: 19910308  
Entered Medline: 19910117

AB Homozygous familial **hypercholesterolemia** (FH) is a serious inherited disease caused by a genetic defect in the cell surface receptor that controls the degradation of low density lipoprotein (LDL). These patients often have myocardial infarction in their teens or early adulthood and are usually unresponsive to drugs. Recently it has been reported promising results using combined drugs regimens in patients with residual receptor activity. We report a new additional patient with receptor-defective homozygous FH treated with a combination of **lovastatin** and **cholestyramine**. The **cholesterol** levels were reduced in a 67% and there were adverse events related to treatment during a 7 month period of follow-up.

CT Check Tags: Case Report; Human; Male  
Child, Preschool  
\***Cholestyramine**: TU, therapeutic use  
Drug Therapy, Combination  
Homozygote  
Hypercholesterolemia, Familial: DT, drug therapy  
\*Hypercholesterolemia, Familial: GE, genetics  
\***Lovastatin**: TU, therapeutic use

RN 11041-12-6 (**Cholestyramine**); 75330-75-5 (**Lovastatin**)

L173 ANSWER 31 OF 63 MEDLINE

AN 91056652 MEDLINE

DN 91056652 PubMed ID: 2123013

TI Reducing high blood **cholesterol** level with drugs.  
Cost-effectiveness of pharmacologic management.

CM Comment in: JAMA. 1991 Apr 17;265(15):1949-50

AU Schulman K A; Kinoshian B; Jacobson T A; Glick H; Willian M K; Koffer H; Eisenberg J M

CS Department of Medicine, Robert Wood Johnson Foundation Clinical Scholars Program, University of Pennsylvania, Philadelphia.

SO JAMA, (1990 Dec 19) 264 (23) 3025-33. Ref: 72  
Journal code: KFR; 7501160. ISSN: 0098-7484.

CY United States

DT Journal; Article; (JOURNAL ARTICLE)  
General Review; (REVIEW)  
(REVIEW, TUTORIAL)

LA English

FS Abridged Index Medicus Journals; Priority Journals

EM 199101

ED Entered STN: 19910222  
Last Updated on STN: 19910222  
Entered Medline: 19910103

AB We performed a cost-effectiveness analysis of pharmacologic treatment of high blood **cholesterol** levels. Agents modeled were **cholestyramine**, colestipol, gemfibrozil, **lovastatin**, niacin, and probucol. Pharmacologic effectiveness was estimated from reported studies. Cost estimates reflect societal resource consumption. Annual costs for therapy ranged from \$327 (niacin) to \$1881 (**lovastatin**, 80 mg/d). Niacin was the most efficient agent for reducing low-density lipoprotein **cholesterol** levels, having an average cost over 5 years of \$139 per percent reduction in low-density lipoprotein **cholesterol** level. **Lovastatin** (20 mg/d) was also efficient (\$177 per percent reduction). **Cholestyramine** was least efficient at \$347. For high-density lipoprotein **cholesterol**, niacin was most efficient, at \$116 per percent increase in high-density lipoprotein **cholesterol** level, followed by gemfibrozil at \$271. Analyses combining low-density lipoprotein **cholesterol** and high-density lipoprotein **cholesterol** effects suggest that niacin and **lovastatin** (20 mg/d) were most efficient for reducing cardiovascular risk.

CT Check Tags: Human; Support, Non-U.S. Gov't  
\***Anticholesteremic Agents**: TU, therapeutic use

**Cholestyramine: TU, therapeutic use**

Clinical Trials

Colestipol: TU, therapeutic use

Cost-Benefit Analysis

**Drug Therapy, Combination**

Gemfibrozil: TU, therapeutic use

**Hypercholesterolemia: DT, drug therapy****\*Hypercholesterolemia: EC, economics****Lovastatin: TU, therapeutic use**

Niacin: TU, therapeutic use

**Probucol: TU, therapeutic use**

Sensitivity and Specificity

RN 11041-12-6 (**Cholestyramine**); 23288-49-5 (Probucol); 25812-30-0  
(Gemfibrozil); 50925-79-6 (Colestipol); 59-67-6 (Niacin); 75330-75-5  
(**Lovastatin**)

CN 0 (**Anticholesteremic Agents**)

L173 ANSWER 32 OF 63 MEDLINE

AN 91056649 MEDLINE

DN 91056649 PubMed ID: 2243428

TI Regression of coronary atherosclerosis during treatment of familial  
**hypercholesterolemia** with combined drug regimens.

CM Comment in: JAMA. 1991 Apr 3;265(13):1688-9

AU Kane J P; Malloy M J; Ports T A; Phillips N R; Diehl J C; Havel R J

CS Cardiovascular Research Institute, University of California, San Francisco  
94143-0130.

NC 5 MO1 RR00079 (NCRR)

HL 14237 (NHLBI)

SO JAMA, (1990 Dec 19) 264 (23) 3007-12.

Journal code: KFR; 7501160. ISSN: 0098-7484.

CY United States

DT (CLINICAL TRIAL)

Journal; Article; (JOURNAL ARTICLE)

(RANDOMIZED CONTROLLED TRIAL)

LA English

FS Abridged Index Medicus Journals; Priority Journals

EM 199101

ED Entered STN: 19910222

Last Updated on STN: 19910222

Entered Medline: 19910103

AB We conducted a randomized, controlled trial in 72 patients with heterozygous familial **hypercholesterolemia** to test whether reducing plasma low-density lipoprotein levels by diet and combined drug regimens can induce regression of coronary lesions. Four hundred fifty-seven lesions were measured before and after a 26-month interval by computer-based quantitative angiography. The primary outcome variable was within-patient mean change in percent area stenosis. Mean low-density lipoprotein **cholesterol** levels decreased from 7.32 +/- 1.5 to 4.45 +/- 1.6 mmol/L. The mean change in percent area stenosis among controls was +0.80, indicating progression, while the mean change for the treatment group was -1.53, indicating regression (P = .039 by two-tailed t test for the difference between groups). Regression among women, analyzed separately, was also significant. The change in percent area stenosis was correlated with low-density lipoprotein levels on trial. We conclude that reduction of low-density lipoprotein **cholesterol** levels can induce regression of atherosclerotic lesions of the coronary arteries in patients with familial **hypercholesterolemia**. The anticipation of benefit from treatment applies to women and men alike.

CT Check Tags: Female; Human; Male; Support, Non-U.S. Gov't; Support, U.S. Gov't, P.H.S.

Adult

Aged

Colestipol: AD, administration & dosage

Coronary Arteriosclerosis: BL, blood

Coronary Arteriosclerosis: DT, drug therapy

\*Coronary Arteriosclerosis: RA, radiography

**Drug Therapy, Combination****Hypercholesterolemia, Familial: BL, blood****\*Hypercholesterolemia, Familial: DT, drug therapy****Lipoproteins, HDL Cholesterol: BL, blood****Lipoproteins, LDL Cholesterol: BL, blood****Lovastatin: AD, administration & dosage**

Middle Age

Niacin: AE, adverse effects

Radiographic Image Interpretation, Computer-Assisted

Triglycerides: BL, blood

RN 50925-79-6 (Colestipol); 59-67-6 (Niacin); 75330-75-5 (Lovastatin)

CN 0 (Lipoproteins, HDL Cholesterol); 0 (Lipoproteins, LDL Cholesterol); 0 (Triglycerides)

L173 ANSWER 33 OF 63 MEDLINE

AN 90385302 MEDLINE

DN 90385302 PubMed ID: 2402652

TI Regression of tendon xanthomas in patients with familial **hypercholesterolemia** treated with **lovastatin**.

AU Illingworth D R; Cope R; Bacon S P

CS Department of Medicine, Oregon Health Sciences University, Portland 97201-3098.

NC HL32271 (NHLBI)

HL37940 (NHLBI)

RR334 (NCRR)

SO SOUTHERN MEDICAL JOURNAL, (1990 Sep) 83 (9) 1053-7.

Journal code: UVH; 0404522. ISSN: 0038-4348.

CY United States

DT Journal; Article; (JOURNAL ARTICLE)

LA English

FS Abridged Index Medicus Journals; Priority Journals

EM 199010

ED Entered STN: 19901122

Last Updated on STN: 19901122

Entered Medline: 19901019

AB Plasma concentrations of total and low-density lipoprotein **cholesterol** are increased twofold to threefold in patients with heterozygous familial **hypercholesterolemia**. This sustained increase leads to accelerated rates of **cholesterol** deposition in the coronary arteries and to the development of tendon xanthomas. To assess whether hypolipidemic therapy with **lovastatin**, alone and in combination therapy with colestipol hydrochloride or nicotinic acid, results in regression of lipid deposits in the tendons of these patients, we have measured Achilles tendon diameters by xeroradiography before and after treatment. In 20 patients treated for a mean of 43 months (during which time plasma **cholesterol** concentrations decreased from 430 to 247 mg/dL), the diameter of both the left and right Achilles tendons measured at three different locations decreased by 0.55 to 1.5 mm. Larger reductions were seen in the tendons of seven of these patients who were treated for a mean of 64 months and whose mean concentrations of **cholesterol** fell from 488 to 279 mg/dL. We conclude that effective long-term hypolipidemic therapy leads to diminution in the size of Achilles tendon xanthomas in patients with heterozygous familial **hypercholesterolemia** and that such therapy is associated with mobilization of tissue stores of **cholesterol** in these patients.

CT Check Tags: Female; Human; Male; Support, U.S. Gov't, P.H.S.

Achilles Tendon: DE, drug effects

Achilles Tendon: RA, radiography

Adult

Colestipol: TU, therapeutic use

**Drug Therapy, Combination****\*Hypercholesterolemia, Familial: DT, drug therapy****Lipoproteins, LDL Cholesterol: BL, blood****\*Lovastatin: TU, therapeutic use**

Middle Age

Niacin: TU, therapeutic use

Remission Induction  
Tendons, Para-Articular: PA, pathology  
\*Wolman Disease: DT, drug therapy  
Wolman Disease: RA, radiography  
RN 50925-79-6 (Colestipol); 59-67-6 (Niacin); 75330-75-5 (Lovastatin)  
CN 0 (Lipoproteins, LDL Cholesterol)

L173 ANSWER 34 OF 63 MEDLINE  
AN 90340166 MEDLINE  
DN 90340166 PubMed ID: 2199801  
TI Comparison of simvastatin and **cholestyramine** in the treatment of  
primary **hypercholesterolaemia**.  
CM Erratum in: Med J Aust 1991 Feb 18;154(4):296  
AU O'Brien R C; Simons L A; Clifton P; Cooper M E; Jennings G L; Jerums G;  
Nestel P J; Sullivan D  
CS Department of Medicine, Austin Hospital, Heidelberg, VIC.  
SO MEDICAL JOURNAL OF AUSTRALIA, (1990 May 7) 152 (9) 480-3.  
Journal code: M26; 0400714. ISSN: 0025-729X.  
CY Australia  
DT (CLINICAL TRIAL)  
Journal; Article; (JOURNAL ARTICLE)  
(MULTICENTER STUDY)  
(RANDOMIZED CONTROLLED TRIAL)  
LA English  
FS Priority Journals  
EM 199009  
ED Entered STN: 19901012  
Last Updated on STN: 19980206  
Entered Medline: 19900907  
AB The effects of simvastatin, a competitive inhibitor of the enzyme  
3-hydroxy-3-methylglutaryl-coenzyme A reductase, on plasma lipid levels  
were compared with those of the bile acid sequestrant  
**cholestyramine** in a randomized parallel study of 60 subjects with  
primary **hypercholesterolaemia**. After a 12-week direct comparison  
period 37 subjects with inadequate **cholesterol** reduction  
received a combination of both drugs and all subjects were followed for a  
further 40 weeks. Simvastatin was more effective than  
**cholestyramine** in lowering total and LDL **cholesterol**  
levels and the LDL/HDL ratio (-31.7% v. -19.7% [P less than 0.01], -41.0%  
v. -31.8% [P less than 0.05] and -46.7% v. -33.6% [P less than 0.01],  
respectively at Week 12). Only simvastatin significantly increased the HDL  
**cholesterol** concentration (+13.3% [P less than 0.01] v. +6.4%).  
**Cholestyramine** increased plasma triglyceride levels by 37.5% (P  
less than 0.01) whereas simvastatin caused a slight non-significant  
reduction. Combined therapy produced a further decrease in total and LDL  
**cholesterol** levels, and in the LDL/HDL ratio, which was sustained  
for the duration of the study. Simvastatin was better tolerated than  
**cholestyramine** (P less than 0.01), and combining the two drugs  
enhanced efficacy without increasing the frequency of side effects.  
CT Check Tags: Comparative Study; Female; Human; Male; Support, Non-U.S.  
Gov't  
Adult  
Aged  
Analysis of Variance  
Anticholesteremic Agents: AD, administration & dosage  
\*Anticholesteremic Agents: TU, therapeutic use  
Australia  
Cholesterol: BL, blood  
Cholestyramine: AD, administration & dosage  
\*Cholestyramine: TU, therapeutic use  
Drug Therapy, Combination  
Follow-Up Studies  
Hydroxymethylglutaryl CoA Reductases: AI, antagonists & inhibitors  
Hypercholesterolemia: BL, blood  
\*Hypercholesterolemia: DT, drug therapy  
Hypercholesterolemia: EN, enzymology



Lovastatin: AD, administration & dosage  
 \*Lovastatin: AA, analogs & derivatives  
 Lovastatin: TU, therapeutic use

Middle Age

Multicenter Studies

Randomized Controlled Trials

**Simvastatin**

Triglycerides: BL, blood

RN 11041-12-6 (**Cholestyramine**); 57-88-5 (**Cholesterol**);  
 75330-75-5 (**Lovastatin**); 79902-63-9 (Simvastatin)  
 CN 0 (**Anticholesteremic Agents**); 0 (Triglycerides); EC 1.1.1.88  
 (Hydroxymethylglutaryl CoA Reductases)

*sequesterant*

L173 ANSWER 35 OF 63 MEDLINE

AN 90287319 MEDLINE

DN 90287319 PubMed ID: 2355995

TI The effects of simvastatin on serum lipoproteins in severe  
**hypercholesterolaemia.**

AU Mol M J; Stuyt P M; Demacker P N; Stalenhoef A F

CS Department of Medicine, University Hospital, Nijmegen.

SO NETHERLANDS JOURNAL OF MEDICINE, (1990 Apr) 36 (3-4) 182-90.

Journal code: NWY; 0356133. ISSN: 0300-2977.

CY Netherlands

DT Journal; Article; (JOURNAL ARTICLE)

LA English

FS Priority Journals

EM 199007

ED Entered STN: 19900824

Last Updated on STN: 19980206

Entered Medline: 19900724

AB The effects of simvastatin, an inhibitor of **cholesterol** synthesis, on serum lipids, lipoprotein composition and apolipoproteins were evaluated in a total of 50 patients with **hypercholesterolaemia**. In the first study, 24 patients (mean serum **cholesterol** 10.74 +/- 1.59 mmol/l) were treated with simvastatin 40 mg daily for 24 wk. Serum **cholesterol** and low density lipoprotein (LDL) **cholesterol** decreased to average values 29-36% and 35-42% below the basal value, respectively. Serum triglycerides decreased by 16-28%, and high density lipoprotein (HDL) **cholesterol** increased by 6-11%. Apolipoprotein A-I concentration increased 6-8% and that of apolipoprotein B decreased 29-33%. The composition of LDL remained unchanged whereas the very low density lipoproteins became enriched in triglycerides. Lipoprotein Lp(a) was not affected. In the second study 26 patients (mean serum **cholesterol** 12.35 +/- 2.05 mmol/l) were treated with simvastatin 40 mg daily as monotherapy or combined with a bile acid binding resin for 2 yr. Serum **cholesterol** levels decreased to values which remained stable throughout the entire study period; after 2 yr this decrease amounted to 43%. Compared to monotherapy, combination therapy yielded a further 12% decrease of **cholesterol**. In the entire group, triglycerides decreased by 16% and HDL **cholesterol** increased by 9%. Side effects were limited to slight increases in alanine aminotransferase and creatine phosphokinase in some patients. Simvastatin appears to be an important asset in the treatment of **hypercholesterolaemia**.

CT Check Tags: Female; Human; Male; Support, Non-U.S. Gov't

Adult

Apolipoproteins: BL, blood

**Cholesterol**: BL, blood

**Cholestyramine**: TU, therapeutic use

Colestipol: TU, therapeutic use

**Drug Therapy, Combination**

\*Hydroxymethylglutaryl CoA Reductases: AI, antagonists & inhibitors

\***Hypercholesterolemia**, Familial: DT, drug therapy

\*Lipoproteins: BL, blood

**Lovastatin**: AE, adverse effects

\***Lovastatin**: AA, analogs & derivatives

**Lovastatin: PD, pharmacology**

**Lovastatin: TU, therapeutic use**

Middle Age

**Simvastatin**

Triglycerides: BL, blood

RN **11041-12-6 (Cholestyramine)**; 50925-79-6 (Colestipol);

**57-88-5 (Cholesterol)**; **75330-75-5 (Lovastatin)**;

79902-63-9 (Simvastatin)

CN 0 (Apolipoproteins); 0 (Lipoproteins); 0 (Triglycerides); EC 1.1.1.88  
(Hydroxymethylglutaryl CoA Reductases)

L173 ANSWER 36 OF 63 MEDLINE

AN 90286050 MEDLINE

DN 90286050 PubMed ID: 2355431

TI Myopathy and rhabdomyolysis associated with **lovastatin**  
-gemfibrozil combination therapy.

CM Comment in: JAMA. 1990 Dec 19;264(23):2991-2

AU Pierce L R; Wysowski D K; Gross T P

CS Division of Metabolism and Endocrine Drug Products, Food and Drug  
Administration, Rockville, MD 20857.

SO JAMA, (1990 Jul 4) 264 (1) 71-5.

Journal code: KFR; 7501160. ISSN: 0098-7484.

CY United States

DT Journal; Article; (JOURNAL ARTICLE)

LA English

FS Abridged Index Medicus Journals; Priority Journals

EM 199007

ED Entered STN: 19900824

Last Updated on STN: 19900824

Entered Medline: 19900720

AB The Food and Drug Administration documents the receipt of 12 case reports of severe myopathy or rhabdomyolysis associated with concomitant use of **lovastatin** and gemfibrozil, including 10 voluntary postmarketing, and 2 required, reports. All patients had serum creatine kinase levels of more than 10,000 U/L, 4 tested showed myoglobinuria, and 5 had acute renal failure. The patients' symptoms resolved when both drugs were discontinued. For the first year of marketing of **lovastatin**, spontaneous reports of myopathy with documentation of creatine kinase level were reviewed for the use of **lovastatin**, gemfibrozil, and combination therapy. The median creatine kinase level in reports involving concomitant **lovastatin** and gemfibrozil use was 15,250 U/L, 20 times that in reports with gemfibrozil use alone and 30 times that in reports with **lovastatin** use alone. Because of the potential for severe myopathy and life-threatening rhabdomyolysis, and given alternative drug combinations for treating hyperlipoproteinemia, the use of **lovastatin** in combination with gemfibrozil is to be discouraged.

CT Check Tags: Case Report; Female; Human; Male

Adult

Aged

Creatine Kinase: BL, blood

Drug Interactions.

**Drug Therapy, Combination**

Gemfibrozil: AD, administration & dosage

\*Gemfibrozil: AE, adverse effects

**Hypercholesterolemia: DT, drug therapy**

Kidney Failure, Acute: CI, chemically induced

**Lovastatin: AD, administration & dosage**

\***Lovastatin: AE, adverse effects**

Middle Age

Muscular Diseases: BL, blood

\*Muscular Diseases: CI, chemically induced

Rhabdomyolysis: BL, blood

\*Rhabdomyolysis: CI, chemically induced

RN 25812-30-0 (Gemfibrozil); **75330-75-5 (Lovastatin)**

CN EC 2.7.3.2 (Creatine Kinase)

L173 ANSWER 37 OF 63 MEDLINE

AN 90282586 MEDLINE

DN 90282586 PubMed ID: 2353864

TI Management of primary mixed hyperlipidemia with **lovastatin**.

AU Vega G L; Grundy S M

CS Department of Clinical Nutrition, University of Texas Southwestern Medical Center, Dallas 75235.

NC HL-29252 (NHLBI)

MO-1RR00633 (NCRR)

SO ARCHIVES OF INTERNAL MEDICINE, (1990 Jun) 150 (6) 1313-9.

Journal code: 7FS; 0372440. ISSN: 0003-9926.

CY United States

DT (CLINICAL TRIAL)

(CONTROLLED CLINICAL TRIAL)

Journal; Article; (JOURNAL ARTICLE)

LA English

FS Abridged Index Medicus Journals; Priority Journals

EM 199007

ED Entered STN: 19900824

Last Updated on STN: 19970203

Entered Medline: 19900718

AB Many patients with high levels of serum total **cholesterol** have a concomitant elevation of serum triglyceride levels and thus have mixed hyperlipidemia. In this study, 13 patients with mixed hyperlipidemia were treated with the **cholesterol**-lowering drug **lovastatin** to determine its effectiveness. In 9 of these patients, **lovastatin** therapy used alone was compared with the drug combination of **lovastatin** and gemfibrozil. In the 13 patients, **lovastatin** therapy produced a 31% reduction in total **cholesterol** level and a 32% decrease in triglyceride levels compared with placebo. It lowered very-low-density plus intermediate-density lipoprotein **cholesterol** levels by 40%, low-density lipoprotein **cholesterol** levels by 36%, and total apolipoprotein B levels by 28%. Concentrations of high-density lipoprotein **cholesterol** and apolipoprotein A-I were unchanged, but total **cholesterol** (and low-density lipoprotein **cholesterol**)/high-density lipoprotein **cholesterol** ratios were markedly reduced. Compared with **lovastatin** alone, **lovastatin** plus gemfibrozil produced greater decreases in very-low-density plus intermediate-density lipoprotein **cholesterol** levels and an increase in high-density lipoprotein **cholesterol** levels, but, in view of the higher risk for severe myopathy with this combination, **lovastatin** used alone may be adequate therapy for many patients with mixed hyperlipidemia.

CT Check Tags: Comparative Study; Human; Male; Support, Non-U.S. Gov't; Support, U.S. Gov't, Non-P.H.S.; Support, U.S. Gov't, P.H.S.

Adult

Aged

**Cholesterol: BL, blood**

**Drug Therapy, Combination**

Gemfibrozil: TU, therapeutic use

**\*Hyperlipidemia: DT, drug therapy**

**Lipoproteins, HDL Cholesterol: BL, blood**

**Lipoproteins, LDL Cholesterol: BL, blood**

**Lipoproteins, VLDL Cholesterol: BL, blood**

**\*Lovastatin: TU, therapeutic use**

Middle Age

Triglycerides: BL, blood

RN 25812-30-0 (Gemfibrozil); 57-88-5 (**Cholesterol**); 75330-75-5 (**Lovastatin**)

CN 0 (Lipoproteins, HDL **Cholesterol**); 0 (Lipoproteins, LDL **Cholesterol**); 0 (Lipoproteins, VLDL **Cholesterol**); 0 (Triglycerides)

L173 ANSWER 38 OF 63 MEDLINE

AN 90265885 MEDLINE

DN 90265885 PubMed ID: 2111917

TI HMG CoA reductase inhibitors as lipid-lowering agents: five years experience with **lovastatin** and an appraisal of simvastatin and pravastatin.

AU Maher V M; Thompson G R

CS MRC Lipoprotein Team, Hammersmith Hospital, London.

SO QUARTERLY JOURNAL OF MEDICINE, (1990 Feb) 74 (274) 165-75.  
Journal code: QKZ; 0401027. ISSN: 0033-5622.

CY ENGLAND: United Kingdom

DT (CLINICAL TRIAL)  
Journal; Article; (JOURNAL ARTICLE)

LA English

FS Priority Journals

EM 199007

ED Entered STN: 19900810  
Last Updated on STN: 19980206  
Entered Medline: 19900703

AB The HMG CoA reductase inhibitors are the most effective drugs for treating **hypercholesterolaemia** currently available. They inhibit **cholesterol** synthesis and thus stimulate receptor-mediated uptake and degradation of low-density lipoprotein **cholesterol** by the liver. In 30 patients with severe **hypercholesterolaemia** administration of **lovastatin** alone or in combination with other lipid-lowering manoeuvres maintained reductions of 25 to 31 per cent in serum **cholesterol** over five years. The drug was easy to take and well tolerated, the only significant side effect being a reversible myopathy. Two similar compounds, simvastatin and pravastatin, exert comparable effects on serum lipids, including modest reductions in triglycerides and increases in high-density lipoprotein **cholesterol**. The use of these drugs seems likely to exert a beneficial effect on atherosclerosis.

CT Check Tags: Comparative Study; Female; Human; Male  
Adult  
Aged  
\*Anticholesteremic Agents: TU, therapeutic use  
Cholestyramine: TU, therapeutic use  
Clinical Trials  
Dose-Response Relationship, Drug  
Drug Therapy, Combination  
Heptanoic Acids: TU, therapeutic use  
\*Hydroxymethylglutaryl CoA Reductases: AI, antagonists & inhibitors  
\*Hypercholesterolemia: DT, drug therapy  
Hypercholesterolemia: GE, genetics  
Lovastatin: AE, adverse effects  
Lovastatin: AA, analogs & derivatives  
Lovastatin: TU, therapeutic use  
Middle Age  
Naphthalenes: TU, therapeutic use  
Phenotype  
Pravastatin  
Simvastatin  
Time Factors

RN 11041-12-6 (Cholestyramine); 75330-75-5 (Lovastatin);  
79902-63-9 (Simvastatin); 81093-37-0 (Pravastatin)

CN 0 (Anticholesteremic Agents); 0 (Heptanoic Acids); 0  
(Naphthalenes); EC 1.1.1.88 (Hydroxymethylglutaryl CoA Reductases)

L173 ANSWER 39 OF 63 MEDLINE

AN 90220330 MEDLINE

DN 90220330 PubMed ID: 2182974

TI The hypolipidemic effects of **lovastatin** and clofibrate alone and in combination in patients with type III hyperlipoproteinemia.

AU Illingworth D R; O'Malley J P

CS Department of Medicine, Oregon Health Sciences University, Portland 97201.

NC HL28399 (NHLBI)  
HL37940 (NHLBI)  
RR334 (NCRR)

SO METABOLISM: CLINICAL AND EXPERIMENTAL, (1990 Apr) 39 (4) 403-9.  
Journal code: MUM; 0375267. ISSN: 0026-0495.

CY United States  
DT (CLINICAL TRIAL)  
Journal; Article; (JOURNAL ARTICLE)  
LA English  
FS Priority Journals  
EM 199005  
ED Entered STN: 19900622  
Last Updated on STN: 19900622  
Entered Medline: 19900515

AB The hypolipidemic effects of **lovastatin** and clofibrate have been evaluated in 12 patients with type III hyperlipoproteinemia. In these patients plasma concentrations of total **cholesterol** decreased from 500 +/- 56 mg/dL (mean +/- SEM) at baseline to 278 +/- 23 mg/dL on **lovastatin** (20 mg twice daily), and were 299 +/- 15 mg/dL during treatment with clofibrate (1 g twice daily). Nine patients were treated sequentially with **lovastatin** at doses of 20 and 40 mg twice daily and clofibrate; in these patients total plasma **cholesterol** concentrations decreased from 549 +/- 67 mg/dL at baseline to 291 +/- 24 mg/dL on **lovastatin** (20 mg twice daily), 247 +/- 20 mg/dL (40 mg twice daily) and were 297 +/- 18 mg/dL on monotherapy with clofibrate. Concentrations of very-low-density lipoprotein (VLDL) **cholesterol** were similar on clofibrate and the higher dose of **lovastatin**, whereas concentrations of low-density lipoprotein (LDL) **cholesterol** were significantly lower on **lovastatin**. In six patients who remained hyperlipidemic on monotherapy with either drug, combination drug therapy with **lovastatin** (20 mg twice daily) plus clofibrate reduced plasma concentrations of total **cholesterol** from 635 +/- 79 mg/dL to 205 +/- 11 mg/dL. No patients were discontinued from single or combined drug therapy and no significant biochemical abnormalities were observed. The results of this study demonstrate the potential usefulness of **lovastatin** in the therapy of type III hyperlipoproteinemia and indicate that, in selected patients who remain **hypercholesterolemic** on monotherapy with either clofibrate or **lovastatin**, combination drug therapy with both of these drugs is effective in further reducing plasma concentrations of total, VLDL, and LDL **cholesterol**. (ABSTRACT TRUNCATED AT 250 WORDS)

CT Check Tags: Comparative Study; Female; Human; Male; Support, U.S. Gov't, P.H.S.  
Adult  
Aged  
Cholesterol: BL, blood  
Clinical Trials  
\*Clofibrate: TU, therapeutic use  
Drug Therapy, Combination  
Follow-Up Studies  
Hyperlipoproteinemia Type III: BL, blood  
\*Hyperlipoproteinemia Type III: DT, drug therapy  
Lipoproteins: BL, blood  
\*Lovastatin: TU, therapeutic use  
Middle Age  
Time Factors  
Triglycerides: BL, blood

RN 57-88-5 (Cholesterol); 637-07-0 (Clofibrate); 75330-75-5 (Lovastatin)

CN 0 (Lipoproteins); 0 (Triglycerides)

L173 ANSWER 40 OF 63 MEDLINE  
AN 90185518 MEDLINE  
DN 90185518 PubMed ID: 2312032  
TI [HMG-CoA reductase inhibitors in familial **hypercholesterolemia**. Therapy with simvastatin alone and in combination with **cholestyramine** in low dosage; a report of 2 years experiences]. HMG-CoA-Reduktase-Inhibitoren bei familiärer **Hypercholesterinämie**. Therapie mit Simvastatin allein und in Kombination mit Colestyramin in

niedriger Dosierung; ein Zwei-Jahres-Erfahrungsbericht.

AU Geisel J; Oette K; Burrichter H  
CS Institut für Klinische Chemie, Universität Köln.  
SO FORTSCHRITTE DER MEDIZIN, (1990 Feb 10) 108 (4) 71-2, 75-6.  
Journal code: F62; 2984763R. ISSN: 0015-8178.  
CY GERMANY, EAST: German Democratic Republic  
DT Journal; Article; (JOURNAL ARTICLE)  
LA German  
FS Priority Journals  
EM 199004  
ED Entered STN: 19900601  
Last Updated on STN: 19980206  
Entered Medline: 19900425

AB We have studied the effect of simvastatin, an inhibitor of the rate-limiting enzyme in **cholesterol** biosynthesis, alone and in combination with **cholestyramine** in 48 patients. Simvastatin 40 mg decreased total serum **cholesterol**, LDL **cholesterol** and apolipoprotein B by 35%, 40% and 35%, respectively, while HDL **cholesterol** and apolipoprotein A-I increased by 10% (p less than 0.01) and 7% (p less than 0.05), respectively. The addition of 8 g **cholestyramine** caused a further decrease in total **cholesterol** and LDL **cholesterol** to a total of 42% and 49%, respectively. Eighteen of the 48 patients have now been under combined treatment for 2 years. The initial high decreases in total **cholesterol** and LDL **cholesterol** were stabilized for the whole period. Some patients developed gastrointestinal complaints, which made necessary a reduction of simvastatin in two cases. Biochemical side effects (e.g. increases in CK and transaminases) were not observed.

CT Check Tags: Female; Human; Male  
Adult  
\*Anticholesteremic Agents: TU, therapeutic use  
\*Cholestyramine: TU, therapeutic use  
Drug Therapy, Combination  
\*Hydroxymethylglutaryl CoA Reductases: AI, antagonists & inhibitors  
\*Hypercholesterolemia, Familial: DT, drug therapy  
\*Lovastatin: AA, analogs & derivatives  
Lovastatin: TU, therapeutic use  
Middle Age  
Simvastatin

RN 11041-12-6 (Cholestyramine); 75330-75-5 (Lovastatin);  
79902-63-9 (Simvastatin)

CN 0 (Anticholesteremic Agents); EC 1.1.1.88 (Hydroxymethylglutaryl CoA Reductases)

L173 ANSWER 41 OF 63 MEDLINE

AN 90184098 MEDLINE  
DN 90184098 PubMed ID: 2178931  
TI Efficacy and safety of simvastatin (alone or in association with **cholestyramine**). A 1-year study in 66 patients with type II hyperlipoproteinaemia.

AU Emmerich J; Aubert I; Bauduceau B; Dachet C; Chanu B; Erlich D; Gautier D; Jacotot B; Rouffy J  
CS Unite de recherches sur les dyslipidemies et l'atherosclerose, INSERM U 32, Hopital Henri Mondor, Creteil, France.  
SO EUROPEAN HEART JOURNAL, (1990 Feb) 11 (2) 149-55.  
Journal code: EM8; 8006263. ISSN: 0195-668X.  
CY ENGLAND: United Kingdom  
DT (CLINICAL TRIAL)  
(CONTROLLED CLINICAL TRIAL)  
Journal; Article; (JOURNAL ARTICLE)  
LA English  
FS Priority Journals  
EM 199004  
ED Entered STN: 19900601  
Last Updated on STN: 19980206  
Entered Medline: 19900424

AB The effects and safety of simvastatin, an inhibitor of 3-hydroxy-3-methylglutaryl coenzyme A reductase, were investigated alone or in association with **cholestyramine** in 66 patients with **hypercholesterolaemia**, in a 1-year study. In type IIa **hypercholesterolaemia** (41 patients), the association was more effective than simvastatin used alone in lowering total **cholesterol** (37% vs 29%) and **LDL-cholesterol** (45% vs 37%). In type IIb **hypercholesterolaemia** (23 patients), the association **simvastatin-cholestyramine** did not appear more effective than simvastatin used alone. The decrease of apoprotein B was parallel to the **LDL-cholesterol** decrease. Apoprotein A1 did not change significantly. The long-term safety of simvastatin was good. No lens opacity was noted. The most serious side-effect in our study was myolysis which occurred in two patients with a marked increase in creatine phosphokinase.

CT Check Tags: Female; Human; Male  
 Adult  
 Aged  
 \*Anticholesteremic Agents: TU, therapeutic use  
 Apoproteins: ME, metabolism  
 \*Cholestyramine: TU, therapeutic use  
 Clinical Trials  
 Drug Therapy, Combination  
 Hypercholesterolemia, Familial: BL, blood  
 \*Hypercholesterolemia, Familial: DT, drug therapy  
 Lipids: BL, blood  
 \*Lovastatin: AA, analogs & derivatives  
 Lovastatin: TU, therapeutic use  
 Middle Age  
 Simvastatin  
 RN 11041-12-6 (Cholestyramine); 75330-75-5 (Lovastatin);  
 79902-63-9 (Simvastatin)  
 CN 0 (Anticholesteremic Agents); 0 (Apoproteins); 0 (Lipids)

L173 ANSWER 42 OF 63 MEDLINE

AN 90154260 MEDLINE  
 DN 90154260 PubMed ID: 2105981  
 TI Silent myocardial ischemia--classification and management.  
 AU Cohn P F  
 CS State University of New York, Stony Brook.  
 SO HOSPITAL PRACTICE (OFFICE EDITION), (1990 Feb 28) 25 (2A) 45-6,  
 48-50.  
 Journal code: HPO; 8404149. ISSN: 8750-2836.  
 CY United States  
 DT Journal; Article; (JOURNAL ARTICLE)  
 LA English  
 FS Abridged Index Medicus Journals; Priority Journals  
 EM 199003  
 ED Entered STN: 19900601  
 Last Updated on STN: 19900601  
 Entered Medline: 19900322

AB As many as 10% of middle-aged men in the United States may have asymptomatic but active coronary artery disease. Additional patients have silent disease after a myocardial infarction or a combination of silent ischemia and angina. Silent and painful episodes have similar hemodynamic and electrical properties, and antianginal medications appear to have global anti-ischemic effects.

CT Check Tags: Case Report; Human; Male  
 Angina Pectoris: PP, physiopathology  
 Atenolol: AD, administration & dosage  
 Drug Therapy, Combination  
 Heart Function Tests  
 Hemodynamics  
 Hypercholesterolemia: DT, drug therapy  
 Hypercholesterolemia: PP, physiopathology  
 Lovastatin: AD, administration & dosage

Middle Age  
\*Myocardial Infarction: DI, diagnosis  
Myocardial Infarction: PP, physiopathology  
Nifedipine: AD, administration & dosage  
Risk Factors

RN 21829-25-4 (Nifedipine); 29122-68-7 (Atenolol); 75330-75-5  
(Lovastatin)

L173 ANSWER 43 OF 63 MEDLINE

AN 90060179 MEDLINE

DN 90060179 PubMed ID: 2511025

TI **Lovastatin** reduces postprandial lipoprotein levels in  
**hypercholesterolaemic** patients with mild hypertriglyceridaemia.

AU Weintraub M S; Eisenberg S; Breslow J L

CS Laboratory of Biochemical Genetics and Metabolism, Rockefeller University,  
New York 10021.

NC HL32435 (NHLBI)

HL33714 (NHLBI)

HL36461 (NHLBI)

+

SO EUROPEAN JOURNAL OF CLINICAL INVESTIGATION, (1989 Oct) 19 (5)  
480-5:

Journal code: EN3; 0245331. ISSN: 0014-2972.

CY ENGLAND: United Kingdom

DT Journal; Article; (JOURNAL ARTICLE)

LA English

FS Priority Journals

EM 199001

ED Entered STN: 19900328

Last Updated on STN: 19970203

Entered Medline: 19900110

AB Drugs that inhibit **cholesterol** synthesis have recently been  
released for lowering LDL-**cholesterol** levels. The current study  
examines the effect of one of these drugs, **lovastatin**, alone and  
in combination with **cholestyramine** on postprandial fat  
metabolism in five patients with severely elevated LDL-**cholesterol**  
and normal triglyceride levels (less than 1.8 mmol l-1) and in five  
patients with similarly elevated LDL-**cholesterol** and mildly  
elevated triglyceride levels (1.8 to 2.7 mmol l-1). In the group of  
patients with normal triglyceride levels, neither **lovastatin**  
alone nor in combination with **cholestyramine** had any effect on  
postprandial lipoprotein levels, while profoundly decreasing LDL-  
**cholesterol** levels. This provides evidence that LDL and  
postprandial lipoproteins are cleared by different mechanisms. In the  
group of five patients with mildly elevated triglyceride levels, in  
addition to LDL-**cholesterol** lowering, **lovastatin**  
significantly lowered VLDL-**cholesterol**, fasting triglyceride and  
postprandial lipoprotein levels. Thus in patients with mild  
hypertriglyceridaemia, **lovastatin** may have another favourable  
effect on the lipoprotein system in addition to LDL-**cholesterol**  
lowering.

CT Check Tags: Female; Human; Male; Support, Non-U.S. Gov't; Support, U.S.  
Gov't, P.H.S.

Adult

Aged

**Cholestyramine**: AD, administration & dosage

**Cholestyramine**: TU, therapeutic use

**Drug Therapy**, Combination

**Hypercholesterolemia**: BL, blood

**Hypercholesterolemia**: CO, complications

\***Hypercholesterolemia**: DT, drug therapy

**Hypertriglyceridemia**: BL, blood

**Hypertriglyceridemia**: CO, complications

\***Hypertriglyceridemia**: DT, drug therapy

\***Lipoproteins**: BL, blood

**Lipoproteins**, LDL **Cholesterol**: BL, blood



**Lipoproteins, VLDL Cholesterol: BL, blood**

**Lovastatin: AD, administration & dosage**

**\*Lovastatin: TU, therapeutic use**

Middle Age

Triglycerides: BL, blood

RN **11041-12-6 (Cholestyramine); 75330-75-5 (Lovastatin)**

CN 0 (Lipoproteins); 0 (Lipoproteins, LDL Cholesterol); 0  
(Lipoproteins, VLDL Cholesterol); 0 (Triglycerides)

L173 ANSWER 44 OF 63 MEDLINE

AN 90039107 MEDLINE

DN 90039107 PubMed ID: 2681508

TI Simvastatin and **cholestyramine** in the long-term treatment of  
**hypercholesterolaemia**.

AU Ytre-Arne K; Nordoy A

CS Department of Medicine, Regionsykehuset i Tromso, Norway.

SO JOURNAL OF INTERNAL MEDICINE, (1989 Nov) 226 (5) 285-90.

Journal code: I2G; 8904841. ISSN: 0954-6820.

CY ENGLAND: United Kingdom

DT (CLINICAL TRIAL)

Journal; Article; (JOURNAL ARTICLE)

(RANDOMIZED CONTROLLED TRIAL)

LA English

FS Priority Journals

EM 198912

ED Entered STN: 19900328

Last Updated on STN: 19980206

Entered Medline: 19891221

AB After 6 weeks on a lipid-lowering diet, 20 outpatients with type II  
hyperlipoproteinaemia (18 type IIa) were randomized to treatment with  
**cholestyramine** 12 g b.i.d. (5 patients) or simvastatin (a new  
HMG-CoA reductase inhibitor) 40 mg q.p.m. (15 patients) for 12 weeks. From  
week 13 to week 20 nine patients in the simvastatin group and all patients  
in the **cholestyramine** group were treated with the combination of  
the two drugs. From week 21 to week 52 all patients were on monotherapy  
with simvastatin. Simvastatin treatment reduced low-density lipoprotein  
(LDL) **cholesterol** by 40% after 12 weeks, compared with 33% in  
the **cholestyramine** group. This difference was not significant.  
The total reductions of LDL-**cholesterol** on combination therapy  
were respectively 60% and 56% in each group. After 52 weeks LDL-  
**cholesterol** was still reduced by 36% (P less than 0.001) on  
monotherapy with simvastatin. Simvastatin also reduced triglycerides (TG)  
by 17% (P less than 0.05) and high-density lipoprotein (HDL)  
**cholesterol** was increased by 19% (P less than 0.01). No serious  
side effects were observed, and the new HMG-CoA reductase inhibitors may  
offer a new approach to the treatment of **hypercholesterolaemia**.

CT Check Tags: Comparative Study; Female; Human; Male

Adult

Aged

Alanine Transaminase: ME, metabolism

**Anticholesteremic Agents: AE, adverse effects**

**\*Anticholesteremic Agents: TU, therapeutic use**

**\*Cholestyramine: TU, therapeutic use**

Clinical Trials

Drug Therapy, Combination

**Hypercholesterolemia: BL, blood**

**\*Hypercholesterolemia: DT, drug therapy**

Lipids: BL, blood

**Lovastatin: AE, adverse effects**

**\*Lovastatin: AA, analogs & derivatives**

**Lovastatin: TU, therapeutic use**

Middle Age

Random Allocation

**Simvastatin**

Time Factors

RN **11041-12-6 (Cholestyramine); 75330-75-5 (Lovastatin);**

79902-63-9 (Simvastatin)  
CN 0 (**Anticholesteremic** Agents); 0 (Lipids); EC 2.6.1.2 (Alanine Transaminase)

L173 ANSWER 45 OF 63 MEDLINE  
AN 90038898 MEDLINE  
DN 90038898 PubMed ID: 2809398  
TI Contrasting effects of **lovastatin** and **cholestyramine** on low-density lipoprotein **cholesterol** and 24-hour urinary mevalonate excretion in patients with heterozygous familial **hypercholesterolemia**.  
AU Pappu A S; Illingworth D R  
CS Department of Medicine, Oregon Health Sciences University, Portland 97201.  
NC HL28399 (NHLBI)  
HL32271 (NHLBI)  
HL37940 (NHLBI)  
+  
SO JOURNAL OF LABORATORY AND CLINICAL MEDICINE, (1989 Nov) 114 (5) 554-62.  
Journal code: IVR; 0375375. ISSN: 0022-2143.  
CY United States  
DT Journal; Article; (JOURNAL ARTICLE)  
LA English  
FS Abridged Index Medicus Journals; Priority Journals  
EM 198912  
ED Entered STN: 19900328  
Last Updated on STN: 19970203  
Entered Medline: 19891215  
AB To further validate the usefulness of quantitative measurements of urinary mevalonic acid excretion as an indicator of rates of **cholesterol** biosynthesis, we have determined the 24-hour urinary excretion of mevalonic acid in patients with heterozygous familial **hypercholesterolemia** treated with drugs that have opposing effects on **cholesterol** biosynthesis. In patients with familial **hypercholesterolemia** treated with the bile acid sequestrant **cholestyramine** (16 gms/day), urinary mevalonate excretion increased by 28%, whereas low-density lipoprotein **cholesterol** concentrations decreased by 21%. In patients with familial **hypercholesterolemia** treated with the 3-hydroxy 3-methyl glutaryl coenzyme A reductase inhibitor **lovastatin** (80 mg/day), concentrations of low-density lipoprotein **cholesterol** and the urinary excretion of mevalonate both decreased (by 40% and 34%, respectively). When **cholestyramine** was used in combination with **lovastatin**, low-density lipoprotein **cholesterol** levels decreased by an additional 14% as compared to monotherapy with **lovastatin**; urinary mevalonate excretion rose by (25%), but the magnitude of this increase was not statistically significant. We conclude that rates of excretion of urinary mevalonic acid (which may reflect rates of whole body **cholesterol** biosynthesis) in patients with FH decrease on therapy with **lovastatin** and increase in response to **cholestyramine** treatment. When used in combination, these drugs counteract each other's effects on **cholesterol** synthesis, but low-density lipoprotein **cholesterol** concentrations decrease further. Measurement of urinary mevalonate excretion affords a practical means of assessing the comparable effects of different dietary or pharmaceutical manipulations on **cholesterol** biosynthesis in human beings.  
CT Check Tags: Female; Human; Male; Support, U.S. Gov't, P.H.S.  
Adult  
Cholestyramine: AD, administration & dosage  
\*Cholestyramine: TU, therapeutic use  
Drug Therapy, Combination  
Heterozygote  
\*Hypercholesterolemia, Familial: DT, drug therapy  
Hypercholesterolemia, Familial: GE, genetics  
Hypercholesterolemia, Familial: ME, metabolism

\*Lipoproteins, LDL Cholesterol: BL, blood

Lovastatin: AD, administration & dosage

\*Lovastatin: TU, therapeutic use

\*Mevalonic Acid: UR, urine

RN 11041-12-6 (Cholestyramine); 150-97-0 (Mevalonic Acid);  
75330-75-5 (Lovastatin)

CN 0 (Lipoproteins, LDL Cholesterol)

L173 ANSWER 46 OF 63 MEDLINE

AN 90023567 MEDLINE

DN 90023567 PubMed ID: 2552800

TI Normalization of LDL receptor function by lymphocytes of patients with heterozygous familial **hypercholesterolemia** after treatment with plasma **cholesterol** lowering agents.

AU Cuthbert J A; East C A; Lipsky P E

CS Department of Internal Medicine, University of Texas Southwestern Medical Center, Dallas.

NC AI-17653 (NIAID)

HL-29252 (NHLBI)

MO1-RR00633 (NCRR)

+

SO AMERICAN JOURNAL OF THE MEDICAL SCIENCES, (1989 Sep) 298 (3)  
152-60.

Journal code: 3L2; 0370506. ISSN: 0002-9629.

CY United States

DT Journal; Article; (JOURNAL ARTICLE)

LA English

FS Abridged Index Medicus Journals; Priority Journals

EM 198910

ED Entered STN: 19900328

Last Updated on STN: 19970203

Entered Medline: 19891031

AB Low density lipoprotein (LDL)-dependent growth of mitogen-activated lymphocytes, inhibited in their capacity to synthesize **cholesterol** endogenously, can be used as an assay of functional receptors for LDL. Using this technique, abnormalities can be detected in circulating lymphocytes obtained from patients with familial **hypercholesterolemia** (FH). Functional lymphocyte LDL receptor activity was decreased in patients with heterozygous FH. Following treatment with the specific inhibitor of **cholesterol** synthesis, **lovastatin**, alone or in combination with a bile acid-binding resin, there was increased expression of functional lymphocyte LDL receptors in five of nine patients. Plasma LDL **cholesterol** levels decreased in all nine patients. Three other patients who were only studied while receiving therapy also manifested increased expression of functional lymphocyte LDL receptors. The degree of improvement in plasma LDL **cholesterol** did not predict the effect on lymphocyte LDL receptor function. Longitudinal studies indicated that an increase in functional LDL receptor activity could be observed with 4 weeks of therapy and persisted for at least 18 months on continuous treatment. These results provide direct evidence that therapy with **lovastatin** and a bile acid-binding resin can lead to increased expression of functional LDL receptors by lymphocytes in the majority (eight of 12) of patients with heterozygous FH.

CT Check Tags: Human; Support, Non-U.S. Gov't; Support, U.S. Gov't, P.H.S.

\*Anticholesteremic Agents: TU, therapeutic use

Cholestyramine: TU, therapeutic use

Colestipol: TU, therapeutic use

Drug Combinations

\*Heterozygote

\*Hypercholesterolemia, Familial: DT, drug therapy

Hypercholesterolemia, Familial: GE, genetics

Hypercholesterolemia, Familial: PP, physiopathology

Lipoproteins

\*Lipoproteins, LDL: ME, metabolism

Lovastatin: TU, therapeutic use

\*Lymphocytes: PH, physiology  
\*Receptors, Cell Surface: PH, physiology  
Receptors, Lipoprotein  
Reference Values  
RN 11041-12-6 (**Cholestyramine**); 50925-79-6 (Colestipol);  
75330-75-5 (**Lovastatin**)  
CN 0 (**Anticholesteremic** Agents); 0 (Drug Combinations); 0  
(Lipoproteins); 0 (Lipoproteins, LDL); 0 (Receptors, Cell Surface); 0  
(Receptors, Lipoprotein)

L173 ANSWER 47 OF 63 MEDLINE  
AN 90023562 MEDLINE  
DN 90023562 PubMed ID: 2801750  
TI Simvastatin: the clinical profile.  
AU Walker J F  
CS Merck Sharp & Dohme Research Laboratories, Rahway, New Jersey 07065.  
SO AMERICAN JOURNAL OF MEDICINE, (1989 Oct 16) 87 (4A) 44S-46S.  
Journal code: 3JU; 0267200. ISSN: 0002-9343.  
CY United States  
DT Journal; Article; (JOURNAL ARTICLE)  
LA English  
FS Abridged Index Medicus Journals; Priority Journals  
EM 198911  
ED Entered STN: 19900328  
Last Updated on STN: 19980206  
Entered Medline: 19891120

AB Simvastatin is the second in the class of compounds known as  
hydroxy-methylglutaryl-coenzyme A reductase inhibitors to be extensively  
studied in humans. The drug has now been given to over 1,800 patients with  
primary **hypercholesterolemia** for periods of up to two years. In  
the range of dosage from 10 to 40 mg once daily, therapy is associated  
with reductions of up to 30 percent in total **cholesterol** and 40  
percent in low-density lipoprotein **cholesterol** levels, as well  
as with increases of approximately 10 percent in high-density lipoprotein  
**cholesterol** levels. The most common clinical adverse experiences  
are mild gastrointestinal effects and headache, which seldom require  
discontinuation of therapy. Elevations of creatine kinase (skeletal muscle  
isoenzyme) levels to more than three times the upper limit of the normal  
range have been seen in about 3 percent of patients, but also have seldom  
required discontinuation of therapy. Conversely, elevations of hepatic  
transaminase levels to more than three times the upper limit of the  
laboratory normal range have been seen in about 1.5 percent of patients  
and have caused discontinuation of therapy in 0.6 percent of patients  
treated. Simvastatin appears to be an effective and well-tolerated agent  
for the treatment of primary **hypercholesterolemia** and, as  
further study confirms long-term safety and efficacy, it should become a  
useful addition to the therapeutic armamentarium.

CT Check Tags: Female; Human; Male  
Aged  
Creatine Kinase: BL, blood  
**Drug Therapy, Combination**  
Eye: DE, drug effects  
\*Hydroxymethylglutaryl CoA Reductases: AI, antagonists & inhibitors  
**\*Hypercholesterolemia: DT, drug therapy**  
**Hypercholesterolemia: EN, enzymology**  
**\*Hypercholesterolemia, Familial: DT, drug therapy**  
Liver: DE, drug effects  
**Lovastatin: AE, adverse effects**  
**\*Lovastatin: AA, analogs & derivatives**  
**Lovastatin: PK, pharmacokinetics**  
**Lovastatin: TU, therapeutic use**  
Middle Age  
**Simvastatin**  
Transaminases: BL, blood  
RN 75330-75-5 (**Lovastatin**); 79902-63-9 (Simvastatin)  
CN EC 1.1.1.88 (Hydroxymethylglutaryl CoA Reductases); EC 2.6.1.

(Transaminases); EC 2.7.3.2 (Creatine Kinase)

L173 ANSWER 48 OF 63 MEDLINE  
 AN 90023561 MEDLINE  
 DN 90023561 PubMed ID: 2679083  
 TI Efficacy and tolerability of simvastatin (MK-733).  
 AU Stalenhoef A F; Mol M J; Stuyt P M  
 CS Department of Internal Medicine, University Hospital Nijmegen, The Netherlands.  
 SO AMERICAN JOURNAL OF MEDICINE, (1989 Oct 16) 87 (4A) 39S-43S.  
 Ref: 16  
 Journal code: 3JU; 0267200. ISSN: 0002-9343.  
 CY United States  
 DT Journal; Article; (JOURNAL ARTICLE)  
 General Review; (REVIEW)  
 (REVIEW, TUTORIAL)  
 LA English  
 FS Abridged Index Medicus Journals; Priority Journals  
 EM 198911  
 ED Entered STN: 19900328  
 Last Updated on STN: 19980206  
 Entered Medline: 19891120  
 AB The efficacy of simvastatin, a new inhibitor of **cholesterol** biosynthesis, was studied in patients with familial **hypercholesterolemia**. A mean reduction in low-density lipoprotein **cholesterol** of 38 percent was observed after eight weeks of treatment with 20 mg of simvastatin; a 42 percent reduction was seen after the next 16 weeks with 40 mg. There was no difference in response whether the drug was taken in one or two doses. In another study, simvastatin (40 mg per day) was compared with **cholestyramine** (8 to 16 g per day). After 12 weeks, low-density lipoprotein **cholesterol** was reduced 43 percent by simvastatin and 29 percent by **cholestyramine**. Combination therapy caused a reduction in low-density lipoprotein **cholesterol** of 54 percent. Simvastatin appeared also to be a potent hypolipidemic drug in 10 patients with familial dysbetalipoproteinemia. The drug was well tolerated. Adverse effects were primarily composed of increases in serum transaminases and creatine phosphokinase. No effects of simvastatin on the production of steroid hormones were observed.  
 CT Check Tags: Female; Human; Male  
 Adrenal Cortex: DE, drug effects  
 Adult  
 Aged  
 \*Anticholesteremic Agents: TU, therapeutic use  
 Cholestyramine: TU, therapeutic use  
 Drug Therapy, Combination  
 \*Hypercholesterolemia, Familial: DT, drug therapy  
 Lipoproteins, LDL Cholesterol: BL, blood  
 Lovastatin: AE, adverse effects  
 \*Lovastatin: AA, analogs & derivatives  
 Lovastatin: TU, therapeutic use  
 Middle Age  
 Simvastatin  
 RN 11041-12-6 (Cholestyramine); 75330-75-5 (Lovastatin);  
 79902-63-9 (Simvastatin)  
 CN 0 (Anticholesteremic Agents); 0 (Lipoproteins, LDL Cholesterol)

L173 ANSWER 49 OF 63 MEDLINE  
 AN 89391895 MEDLINE  
 DN 89391895 PubMed ID: 2675812  
 TI Simvastatin (MK 733): an effective treatment for **hypercholesterolemia**.  
 AU Lintott C J; Scott R S; Nye E R; Robertson M C; Sutherland W H  
 CS Department of Medicine, Princess Margaret Hospital, Christchurch, New Zealand.

SO AUSTRALIAN AND NEW ZEALAND JOURNAL OF MEDICINE, (1989 Aug) 19  
(4) 317-20.  
Journal code: 9H9; 1264322. ISSN: 0004-8291.

CY Australia  
DT (CLINICAL TRIAL)  
Journal; Article; (JOURNAL ARTICLE)  
(RANDOMIZED CONTROLLED TRIAL)

LA English  
FS Priority Journals  
EM 198910  
ED Entered STN: 19900309  
Last Updated on STN: 19980206  
Entered Medline: 19891019

AB This study describes the efficacy of the drug simvastatin. It is likely to be the first HMG CoA reductase inhibitor in Australia and New Zealand available for the treatment of hyperlipidemia. Twenty-four patients, 12 men and 12 women with primary **hypercholesterolemia** were randomly allocated to treatment by **cholestyramine** (eight patients) or to simvastatin (16 patients) for a 12-week period. With simvastatin, total **cholesterol** levels decreased by 37.5% from a baseline mean of 10.33 mmol/L to 6.4 mmol/L after 12 weeks. Low density lipoprotein (LDL) **cholesterol** concentration decreased by 48.2% from 8.40 mmol/L to 4.39 mmol/L. These effects were better than observed for **cholestyramine** alone where **cholesterol** and LDL-**cholesterol** reductions were 24.9% and 33.1% respectively. Thirteen patients, however, did not achieve target LDL levels of 3.62 mmol/L, or below, and therefore were treated with a combination of **cholestyramine** and simvastatin, resulting in a decrease of total **cholesterol** and LDL-**cholesterol** by 45.5% and 53.5% of baseline values studied over an eight-week period. No major clinical side-effects were encountered. One patient appeared to have had a change in colour vision at the end of the study at 20 weeks, without loss of visual acuity.

CT Check Tags: Female; Human; Male  
Adult  
Aged  
Anticholesteremic Agents: AD, administration & dosage  
\*Anticholesteremic Agents: TU, therapeutic use  
Cholesterol: BL, blood  
Cholestyramine: AD, administration & dosage  
Cholestyramine: TU, therapeutic use  
Clinical Trials  
Drug Therapy, Combination  
Hypercholesterolemia: BL, blood  
\*Hypercholesterolemia: DT, drug therapy  
Lipoproteins, LDL Cholesterol: BL, blood  
Lovastatin: AD, administration & dosage  
\*Lovastatin: AA, analogs & derivatives  
Lovastatin: TU, therapeutic use  
Middle Age  
Random Allocation  
Simvastatin

RN 11041-12-6 (Cholestyramine); 57-88-5 (Cholesterol);  
75330-75-5 (Lovastatin); 79902-63-9 (Simvastatin)

CN 0 (Anticholesteremic Agents); 0 (Lipoproteins, LDL Cholesterol)

L173 ANSWER 50 OF 63 MEDLINE  
AN 89182068 MEDLINE  
DN 89182068 PubMed ID: 2927555  
TI [Efficacy and safety of simvastatin, a new **cholesterol**-lowering drug].  
Effectiviteit en veiligheid van simvastatine, een nieuw **cholesterolverlagend** geneesmiddel.  
AU Mol M J; Stuyt P M; Stalenhoef A F  
SO NEDERLANDS TIJDSCHRIFT VOOR GENEESKUNDE, (1989 Feb 18) 133 (7)

362-6.  
Journal code: NUK; 0400770. ISSN: 0028-2162.  
CY Netherlands  
DT Journal; Article; (JOURNAL ARTICLE)  
LA Dutch  
FS Priority Journals  
EM 198905  
ED Entered STN: 19900306  
Last Updated on STN: 19980206  
Entered Medline: 19890511  
AB The effects of simvastatin, an inhibitor of **cholesterol** synthesis, was studied in 50 patients with **hypercholesterolaemia**. In the first study, 24 patients with serum **cholesterol** levels of 10.74 +/- 1.59 mmol/l were treated with simvastatin 40 mg daily for 6 months. Serum **cholesterol** levels decreased within 4 to 8 weeks to stable values 30 to 36% below the basal value. Serum triglycerides decreased by 16 to 28% and high density lipoprotein (HDL) **cholesterol** increased by 6 to 11% on average. In the second study, 26 patients with serum **cholesterol** levels of 12.35 +/- 2.05 mmol/l were treated with simvastatin 40 mg daily as monotherapy or combined with a bile acid binding resin for 2 years. **Cholesterol** levels decreased to values which remained stable throughout the entire study period; after 2 years the decrease amounted to 43%. Compared with monotherapy, combination with a bile acid binding resin yielded a further 12% decrease of **cholesterol**. In the entire group, triglycerides decreased by 16% and HDL **cholesterol** increased by 9% on the average. Side effects were limited to slight increases in alanine aminotransferase and creatine phosphokinase occurring in some patients. Simvastatin appears to be an important asset in the treatment of **hypercholesterolaemia**.  
CT Check Tags: Female; Human; Male  
    \*Anticholesteremic Agents: TU, therapeutic use  
    Cholesterol: BL, blood  
    Cholestyramine: AD, administration & dosage  
    Drug Therapy, Combination  
    \*Hydroxymethylglutaryl CoA Reductases: AI, antagonists & inhibitors  
    \*Hypercholesterolemia: DT, drug therapy  
    Lovastatin: AD, administration & dosage  
    Lovastatin: AE, adverse effects  
    \*Lovastatin: AA, analogs & derivatives  
    Lovastatin: TU, therapeutic use  
    Middle Age  
    Simvastatin  
RN 11041-12-6 (Cholestyramine); 57-88-5 (Cholesterol);  
75330-75-5 (Lovastatin); 79902-63-9 (Simvastatin)  
CN 0 (Anticholesteremic Agents); EC 1.1.1.88 (Hydroxymethylglutaryl CoA Reductases)  
  
L173 ANSWER 51 OF 63 MEDLINE  
AN 89136172 MEDLINE  
DN 89136172 PubMed ID: 2645064  
TI Influence of **lovastatin** plus gemfibrozil on plasma lipids and lipoproteins in patients with heterozygous familial **hypercholesterolemia**.  
AU Illingworth D R; Bacon S  
CS Department of Medicine, Oregon Health Sciences University, Portland 97201.  
NC HL-32271 (NHLBI)  
HL-37940 (NHLBI)  
RR334 (NCRR)  
SO CIRCULATION, (1989 Mar) 79 (3) 590-6.  
Journal code: DAW; 0147763. ISSN: 0009-7322.  
CY United States  
DT (CLINICAL TRIAL)  
Journal; Article; (JOURNAL ARTICLE)  
LA English  
FS Abridged Index Medicus Journals; Priority Journals

EM 198904  
ED Entered STN: 19900306  
Last Updated on STN: 19970203  
Entered Medline: 19890406  
AB We investigated the **hypcholesterolemic** effects of **lovastatin** alone and in combination with gemfibrozil on plasma lipids and lipoproteins in 12 adult patients with well-characterized heterozygous familial **hypercholesterolemia**. Plasma concentrations of low density lipoprotein (LDL) **cholesterol** decreased from 321 +/- 14 mg/dl on diet only to 207 +/- 8 mg/dl (-35.5%) on single-drug therapy with **lovastatin** at a dose of 40 mg twice daily, whereas triglyceride concentrations fell by 27.6% (from 145 +/- 20 to 105 +/- 20 mg/dl). Subsequent addition of gemfibrozil at a dose of 600 mg twice daily resulted in a nonsignificant further reduction in LDL **cholesterol** to 194 +/- 7 mg/dl (-39.6% change from baseline), whereas triglycerides decreased to 80 mg/dl (-44.8%, p less than 0.05 vs. single-drug therapy with **lovastatin**). Plasma concentrations of high density lipoprotein (HDL) increased slightly during **lovastatin** and combined drug therapy (from 45 +/- 4 mg/dl at baseline to 46 +/- 4 mg/dl on **lovastatin** to 48 +/- 4 mg/dl on **lovastatin** plus gemfibrozil). The response to combination drug therapy in individual patients was heterogeneous and clinically significant decreases in LDL **cholesterol** concentrations were noted in two of the 12 patients, whereas in three patients LDL **cholesterol** concentrations increased on the combined drug regimen. One patient developed an asymptomatic increase in creatine kinase on monotherapy with **lovastatin** and a more pronounced and symptomatic increase during combination drug therapy with **lovastatin** plus gemfibrozil. (ABSTRACT TRUNCATED AT 250 WORDS)  
CT Check Tags: Comparative Study; Female; Human; Male; Support, U.S. Gov't, P.H.S.  
Adult  
Clinical Trials  
Drug Therapy, Combination  
\*Gemfibrozil: TU, therapeutic use  
Heterozygote  
Hypercholesterolemia, Familial: BL, blood  
\*Hypercholesterolemia, Familial: DT, drug therapy  
Lipoproteins, HDL Cholesterol: BL, blood  
Lipoproteins, LDL Cholesterol: BL, blood  
\*Lovastatin: TU, therapeutic use  
Middle Age  
Triglycerides: BL, blood  
RN 25812-30-0 (Gemfibrozil); 75330-75-5 (Lovastatin)  
CN 0 (Lipoproteins, HDL Cholesterol); 0 (Lipoproteins, LDL Cholesterol); 0 (Triglycerides)  
  
L173 ANSWER 52 OF 63 MEDLINE  
AN 89104816 MEDLINE  
DN 89104816 PubMed ID: 2492189  
TI Treatment of heterozygous familial **hypercholesterolemia** with lipid-lowering drugs.  
AU Illingworth D R; Bacon S  
CS Department of Medicine, Oregon Health Sciences University, Portland 97201.  
NC HL28399 (NHLBI)  
HL32271 (NHLBI)  
HL37940 (NHLBI)  
+  
SO ARTERIOSCLEROSIS, (1989 Jan-Feb) 9 (1 Suppl) I121-34. Ref: 73  
Journal code: 89S; 8401388. ISSN: 0276-5047.  
CY United States  
DT Journal; Article; (JOURNAL ARTICLE)  
General Review; (REVIEW)  
(REVIEW, TUTORIAL)  
LA English  
FS Priority Journals



EM 198902  
ED Entered STN: 19900308  
Last Updated on STN: 19980206  
Entered Medline: 19890222  
AB Patients with heterozygous familial **hypercholesterolemia** (FH) constitute a unique population at high risk for the premature development of coronary artery disease (CAD) and in whom long-term **hypcholesterolemic** therapy to reduce elevated levels of low density lipoprotein (LDL) **cholesterol** is most clearly indicated. Optimal therapy invariably requires diet regulation plus hypolipidemic drug therapy. When used as single agents, the bile-acid sequestrants, **cholestyramine** and colestipol, lower LDL **cholesterol** concentrations by 20% to 35% in compliant patients, whereas decreases of 20% to 30% can be achieved with nicotinic acid in doses of 3 to 6 g/day. Bezafibrate, fenofibrate, and ciprofibrate have also been shown to lower LDL **cholesterol** levels by 20% to 30%, and these drugs are more effective than gemfibrozil and clofibrate. Probucol, neomycin, and D-thyroxine reduce LDL **cholesterol** concentrations by 10% to 15% in single-drug use. Clinical trials with a new class of drugs that inhibit the rate-limiting enzyme in **cholesterol** biosynthesis, 3-hydroxy-3-methylglutaryl coenzyme A (HMG CoA) reductase, and that includes **lovastatin**, simvastatin, and pravastatin indicate that these drugs lower LDL **cholesterol** concentrations by 30% to 50% in patients with heterozygous FH. Combined drug therapy with a bile-acid sequestrant and nicotinic acid lowers LDL **cholesterol** by 40% to 55%, whereas fenofibrate, bezafibrate, or probucol plus a bile-acid sequestrant results in reductions varying from 25% to 50%. The combinations of an HMG CoA reductase inhibitor with either a bile-acid sequestrant or nicotinic acid appears to be the most promising, and these regimens reduce LDL **cholesterol** levels by 45% to 60%. With appropriate use, the currently available **hypcholesterolemic** drugs have the potential to markedly change the natural history of premature atherosclerosis that occurs in untreated patients with FH.

CT Check Tags: Human; Support, U.S. Gov't, P.H.S.  
Butyrates: TU, therapeutic use  
**Cholestyramine: TU, therapeutic use**  
Colestipol: TU, therapeutic use  
**Drug Therapy, Combination**  
Gemfibrozil: TU, therapeutic use  
Heptanoic Acids: TU, therapeutic use  
Heterozygote  
Hydroxymethylglutaryl CoA Reductases: AI, antagonists & inhibitors  
**\*Hypercholesterolemia, Familial: DT, drug therapy**  
**Lovastatin: AA, analogs & derivatives**  
**Lovastatin: TU, therapeutic use**  
Naphthalenes: TU, therapeutic use  
Neomycin: TU, therapeutic use  
Niacin: TU, therapeutic use  
**Pravastatin**  
**Probucol: TU, therapeutic use**  
**Simvastatin**  
Thyroxine: TU, therapeutic use

RN 11041-12-6 (**Cholestyramine**); 1404-04-2 (Neomycin); 23288-49-5 (Probucol); 25812-30-0 (Gemfibrozil); 50925-79-6 (Colestipol); 59-67-6 (Niacin); 7488-70-2 (Thyroxine); 75330-75-5 (**Lovastatin**); 79902-63-9 (Simvastatin); 81093-37-0 (Pravastatin)

CN 0 (Butyrates); 0 (Heptanoic Acids); 0 (Naphthalenes); EC 1.1.1.88 (Hydroxymethylglutaryl CoA Reductases)

L173 ANSWER 53 OF 63 MEDLINE  
AN 89090090 MEDLINE  
DN 89090090 PubMed ID: 2642754  
TI Intensive combination drug therapy of familial **hypercholesterolemia** with **lovastatin**, probucol, and colestipol hydrochloride.  
AU Witztum J L; Simmons D; Steinberg D; Beltz W F; Weinreb R; Young S G;

Lester P; Kelly N; Juliano J  
CS Department of Medicine, University of California, San Diego, La Jolla  
92093-0613.  
NC HL-14197 (NHLBI)  
PHS-RR-00827 (NCRR)  
SO CIRCULATION, (1989 Jan) 79 (1) 16-28.  
Journal code: DAW; 0147763. ISSN: 0009-7322.  
CY United States  
DT (CLINICAL TRIAL)  
(CONTROLLED CLINICAL TRIAL)  
Journal; Article; (JOURNAL ARTICLE)  
LA English  
FS Abridged Index Medicus Journals; Priority Journals  
EM 198902  
ED Entered STN: 19900308  
Last Updated on STN: 19970203  
Entered Medline: 19890222  
AB Patients with familial **hypercholesterolemia** (FH) have had a  
life-long sustained elevation of low-density lipoprotein (LDL)  
**cholesterol** levels. Consequently, there is a need to maximally  
lower their elevated levels, and this usually requires lowering LDL levels  
more than 50%. Because no single hypolipidemic drug will consistently  
produce such degrees of lowering, combination drug therapy with two or  
even three agents is required to produce the desired degree of  
**cholesterol** lowering. A prospective trial was designed to  
determine if combination therapy using three hypolipidemic agents could  
effectively lower LDL levels in 17 severely affected FH subjects.  
Colestipol hydrochloride (10 g b.i.d.), probucol (500 mg b.i.d.), and  
**lovastatin** (20 or 40 mg b.i.d.) were given to each patient, in  
varying combinations, over a 25-month period. **Lovastatin** (40  
mg/day) uniformly lowered LDL levels 36%. Probucol lowered LDL only 14%  
and in a variable manner. The combination of **lovastatin** and  
probucol lowered LDL no better than **lovastatin** alone.  
**Lovastatin** plus colestipol lowered LDL 52%; probucol added as a  
third agent produced no further lowering. **Lovastatin** (80 mg/day)  
plus colestipol lowered LDL 56%. **Lovastatin** increased  
high-density lipoprotein (HDL) **cholesterol** levels 6%, whereas  
probucol decreased HDL 29%. In all patients there was an effective  
lowering of LDL levels, ranging from 40% to 70%. Thus, **lovastatin**  
plus colestipol is an effective hypolipidemic regimen for producing marked  
decreases in LDL levels in FH subjects. The addition of probucol as a  
third hypolipidemic agent adds little to the therapeutic regimen as  
measured by lowering of LDL levels.  
CT Check Tags: Human; Support, Non-U.S. Gov't; Support, U.S. Gov't, P.H.S.  
**Cholesterol: BL, blood**  
Clinical Trials  
Colestipol: AE, adverse effects  
\*Colestipol: TU, therapeutic use  
Drug Interactions  
**Drug Therapy, Combination**  
**Hypercholesterolemia, Familial: BL, blood**  
\***Hypercholesterolemia, Familial: DT, drug therapy**  
**Lipoproteins, HDL: BL, blood**  
**Lipoproteins, LDL: BL, blood**  
**Lovastatin: AE, adverse effects**  
\***Lovastatin: TU, therapeutic use**  
\*Phenols: TU, therapeutic use  
\*Polyamines: TU, therapeutic use  
**Probucol: AE, adverse effects**  
\***Probucol: TU, therapeutic use**  
Prospective Studies  
Triglycerides: BL, blood  
Xanthomatosis: BL, blood  
RN 23288-49-5 (Probucol); 50925-79-6 (Colestipol); 57-88-5  
(**Cholesterol**); 75330-75-5 (**Lovastatin**)  
CN 0 (Lipoproteins, HDL); 0 (Lipoproteins, LDL); 0 (Phenols); 0 (Polyamines);

## 0 (Triglycerides)

L173 ANSWER 54 OF 63 MEDLINE

AN 89050411 MEDLINE

DN 89050411 PubMed ID: 3056429

TI Effects of **lovastatin** alone and in combination with **cholestyramine** on serum lipids and apolipoproteins in heterozygotes for familial **hypercholesterolemia**.

AU Leren T P; Hjermann I; Berg K; Leren P; Foss O P; Viksmoen L

CS Medical Out-Patient Clinic, Ulleval Hospital, Oslo, Norway.

SO ATHEROSCLEROSIS, (1988 Oct) 73 (2-3) 135-41.

Journal code: 95X; 0242543. ISSN: 0021-9150.

CY Netherlands

DT (CLINICAL TRIAL)

Journal; Article; (JOURNAL ARTICLE)

LA English

FS Priority Journals

EM 198812

ED Entered STN: 19900308

Last Updated on STN: 19900308

Entered Medline: 19881207

AB We have studied the effect of **lovastatin**, an inhibitor of the rate-limiting enzyme in **cholesterol** biosynthesis (3-hydroxy-3-methylglutaryl coenzyme A reductase), alone and in combination with the bile acid sequestrant **cholestyramine** on lipid parameters in 30 heterozygous patients with familial **hypercholesterolemia** (FH) during a 20-week open trial. **Lovastatin** 40 mg bid (twice daily) decreased significantly total serum **cholesterol**, low density lipoprotein (LDL)-**cholesterol**, triglycerides and apolipoprotein B by 36%, 45%, 29% and 11%, respectively, while high density lipoprotein (HDL)-**cholesterol** and apolipoprotein A-I were increased significantly by 16% and 37%, respectively. These data are consistent with a reduction in both the number of LDL particles and in their **cholesterol** content. Addition of **cholestyramine** 4 g bid caused a significant further decrease in total serum **cholesterol** and LDL-**cholesterol** to a total of 43% and 61%, respectively. The addition of 4 g bid or 8 g bid of **cholestyramine** caused only minor changes in the other lipid parameters. No effect was found by these drugs on Lp(a) lipoprotein level. We conclude that **lovastatin** alone or in combination with a small dose of **cholestyramine** normalizes the lipid profile in most FH heterozygotes.

CT Check Tags: Female; Human; Male; Support, Non-U.S. Gov't Adult

\*Apolipoproteins: BL, blood

\***Cholestyramine**: AD, administration & dosage**Cholestyramine**: AE, adverse effects**Cholestyramine**: TU, therapeutic use

Clinical Trials

Drug Therapy, Combination

Heterozygote

**Hypercholesterolemia, Familial**: BL, blood\***Hypercholesterolemia, Familial**: DT, drug therapy**Hypercholesterolemia, Familial**: GE, genetics

\*Lipids: BL, blood

\***Lovastatin**: AD, administration & dosage**Lovastatin**: AE, adverse effects**Lovastatin**: TU, therapeutic use

Middle Age

RN 11041-12-6 (**Cholestyramine**); 75330-75-5 (**Lovastatin**)

CN 0 (Apolipoproteins); 0 (Lipids)

L173 ANSWER 55 OF 63 MEDLINE

AN 88239259 MEDLINE

DN 88239259 PubMed ID: 3288029

TI Combination drug therapy for familial combined hyperlipidemia.

AU East C; Bilheimer D W; Grundy S M  
CS University of Texas Southwestern Medical Center, Dallas.  
NC AM 07307 (NIADDK)  
HL 29252 (NHLBI)  
MO1-RR00633 (NCRR)  
SO ANNALS OF INTERNAL MEDICINE, (1988 Jul 1) 109 (1) 25-32.  
Journal code: 5A6; 0372351. ISSN: 0003-4819.  
CY United States  
DT (CLINICAL TRIAL)  
Journal; Article; (JOURNAL ARTICLE)  
(RANDOMIZED CONTROLLED TRIAL)  
LA English  
FS Abridged Index Medicus Journals; Priority Journals  
EM 198807  
ED Entered STN: 19900308  
Last Updated on STN: 19970203  
Entered Medline: 19880711  
AB STUDY OBJECTIVE: To compare the efficacy of gemfibrozil and colestipol with gemfibrozil and **lovastatin** in patients with familial combined hyperlipidemia. DESIGN: A prospective, randomized trial. SETTING: An outpatient clinical research center in a tertiary care center. PATIENTS: Seventeen patients with familial combined hyperlipidemia documented by studies of first-degree relatives; nine patients with type 2b hyperlipoproteinemia, and eight patients with type 4 hyperlipoproteinemia. INTERVENTIONS: Baseline lipid, lipoprotein, and apolipoprotein levels were obtained during control periods on diet alone and on gemfibrozil therapy. Patients then received gemfibrozil and colestipol or gemfibrozil and **lovastatin** in a randomized order. MEASUREMENTS AND MAIN RESULTS: In patients with type 2b hyperlipoproteinemia, gemfibrozil alone significantly reduced total **cholesterol** by 11%, and low density lipoprotein (LDL)-apolipoprotein B by 18%, did not change LDL-**cholesterol**, and raised high density lipoprotein (HDL)-**cholesterol** levels by 26%. Addition of either colestipol or **lovastatin** reduced LDL-**cholesterol** levels by 17% and 25%, respectively, compared to gemfibrozil alone. However, colestipol mitigated the HDL-**cholesterol** raising effect of gemfibrozil and did not further reduce LDL-apolipoprotein B levels. In contrast, addition of **lovastatin** caused an additional reduction of LDL-apolipoprotein B 19% compared with gemfibrozil alone. In patients with type 4 hyperlipoproteinemia, gemfibrozil alone reduced triglycerides by 40%, raised HDL-**cholesterol** by 26%, and increased LDL-**cholesterol** levels by 29%. The addition of either colestipol or **lovastatin** reduced LDL-**cholesterol** levels by 34% and 33%, respectively (compared with gemfibrozil alone), but greater reductions of LDL-apolipoprotein B (30% with **lovastatin** compared with 15% with colestipol, compared with gemfibrozil alone), and increases in HDL-**cholesterol** levels (8% increase with **lovastatin** compared with 10% decrease with colestipol, compared to gemfibrozil alone) were seen with the **lovastatin** combination. CONCLUSIONS: Although gemfibrozil with either colestipol or **lovastatin** favorably altered lipoprotein levels in patients with hypertriglyceridemia and familial combined hyperlipidemia, the combination of gemfibrozil and **lovastatin** appeared superior overall.  
CT Check Tags: Comparative Study; Female; Human; Male; Support, Non-U.S. Gov't; Support, U.S. Gov't, P.H.S.  
Adult  
\*Antilipemic Agents: TU, therapeutic use  
Cholelithiasis: DI, diagnosis  
\*Colestipol: TU, therapeutic use  
Drug Therapy, Combination  
Gemfibrozil  
Hypercholesterolemia, Familial: DT, drug therapy  
Hyperlipidemia, Familial Combined: BL, blood  
\*Hyperlipidemia, Familial Combined: DT, drug therapy  
Hyperlipoproteinemia Type IV: DT, drug therapy

**\*Lovastatin: TU, therapeutic use**

Middle Age

**\*Pentanoic Acids: TU, therapeutic use****\*Polyamines: TU, therapeutic use**

Random Allocation

Ultrasonography

**\*Valerates: TU, therapeutic use**RN 25812-30-0 (Gemfibrozil); 50925-79-6 (Colestipol); **75330-75-5****(Lovastatin)**

CN 0 (Antilipemic Agents); 0 (Pentanoic Acids); 0 (Polyamines); 0 (Valerates)

L173 ANSWER 56 OF 63 MEDLINE

AN 88022223 MEDLINE

DN 88022223 PubMed ID: 3662275

TI Complementarity of colestipol, niacin, and **lovastatin** in treatment of severe familial **hypercholesterolemia**.

AU Malloy M J; Kane J P; Kunitake S T; Tun P

CS Cardiovascular Research Institute, University of California, San Francisco.

NC HL 14237 (NHLBI)

HL 31210 (NHLBI)

RR-79 (NCRR)

+

SO ANNALS OF INTERNAL MEDICINE, (1987 Nov) 107 (5) 616-23.

Journal code: 5A6; 0372351. ISSN: 0003-4819.

CY United States

DT Journal; Article; (JOURNAL ARTICLE)

LA English

FS Abridged Index Medicus Journals; Priority Journals

EM 198711

ED Entered STN: 19900305

Last Updated on STN: 19970203

Entered Medline: 19871120

AB OBJECTIVE: To compare the effectiveness of the ternary-drug combination of colestipol, niacin, and **lovastatin** with binary combinations of those drugs in treating patients with familial **hypercholesterolemia**. DESIGN: An open sequential study of serum lipoprotein responses in patients receiving diet alone (mean duration, 4 months); colestipol and niacin with diet (mean duration, 9 months); and colestipol, niacin, and **lovastatin** with diet (mean duration, 15 months). SETTING: Metabolic ward and lipid clinic of a university medical center. PATIENTS: Twenty-two patients with clinical characteristics of familial **hypercholesterolemia** (low-density-lipoprotein **cholesterol**, greater than 8.48 mmol/L; 21 of 22 with tendon xanthomas). INTERVENTIONS: Diet: less than 200 mg/d of **cholesterol** and less than 8% of total calories from saturated fat; colestipol, 30 g/d; **lovastatin**, 40 to 60 mg/d; and niacin, 1.5 to 7.5 g/d. MEASUREMENTS AND MAIN RESULTS: Mean total serum **cholesterol** and low-density-lipoprotein **cholesterol** levels of 4.86 +/- 0.62 mmol/L (188 +/- 24 mg/dL SD) and 2.89 +/- 0.54 mmol/L (112 +/- 21 mg/dL SD), respectively, were significantly lower during ternary-drug treatment than during colestipol-niacin treatment (p less than 0.003) or during treatment in which other possible binary combinations were given. The **cholesterol** content of very low-density-lipoproteins was lower and high-density-lipoprotein **cholesterol** levels higher during this phase than during the colestipol-niacin phase. CONCLUSIONS: Colestipol, **lovastatin**, and niacin are mutually complementary in treating **hypercholesterolemia**. This regimen produces reductions in serum **cholesterol** levels similar to those associated with regression of atheromatous plaques in animal studies.

CT Check Tags: Female; Human; Male; Support, Non-U.S. Gov't; Support, U.S. Gov't, P.H.S.

Adult

Aged

Apolipoproteins B: BL, blood

**Cholesterol: BL, blood**

\*Colestipol: AD, administration & dosage  
    **Drug Therapy, Combination**  
    Heterozygote  
    Homozygote  
    \*Hypercholesterolemia, Familial: DT, drug therapy  
    Hypercholesterolemia, Familial: GE, genetics  
    Lipoproteins, LDL Cholesterol: BL, blood  
    \*Lovastatin: AD, administration & dosage  
    Middle Age  
\*Niacin: AD, administration & dosage  
\*Polyamines: AD, administration & dosage  
RN 50925-79-6 (Colestipol); 57-88-5 (Cholesterol); 59-67-6  
    (Niacin); 75330-75-5 (Lovastatin)  
CN 0 (Apolipoproteins B); 0 (Lipoproteins, LDL Cholesterol); 0  
    (Polyamines)

L173 ANSWER 57 OF 63 MEDLINE  
AN 87153126 MEDLINE  
DN 87153126 PubMed ID: 3644588  
TI Comparison of six pharmacologic regimens for **hypercholesterolemia**

AU Hoeg J M; Maher M B; Bailey K R; Brewer H B Jr  
SO AMERICAN JOURNAL OF CARDIOLOGY, (1987 Apr 1) 59 (8) 812-5.  
Journal code: 3DQ; 0207277. ISSN: 0002-9149.  
CY United States  
DT Journal; Article; (JOURNAL ARTICLE)  
LA English  
FS Abridged Index Medicus Journals; Priority Journals  
EM 198704  
ED Entered STN: 19900303  
Last Updated on STN: 19900303  
Entered Medline: 19870423

AB Six sequential clinical trials were conducted over 5 years to evaluate the safety and efficacy of different treatment regimens for **hypercholesterolemia**. Of all the study participants, 11 patients were evaluated in all 6 clinical trials using the following regimens: neomycin, neomycin/niacin, **cholestyramine**, **cholestyramine**/neomycin, **lovastatin** and **lovastatin**/neomycin. All 6 regimens significantly (p less than 0.05) reduced both total and low-density lipoprotein **cholesterol** concentrations by 25 to 42% from baseline levels. Only neomycin/niacin, **cholestyramine** and **lovastatin** significantly increased the high-density lipoprotein (HDL) **cholesterol** concentration, reducing the total **cholesterol**/high-density lipoprotein **cholesterol** ratio to less than 4.7. Thus, all 6 tested regimens were effective in modifying the plasma lipoprotein concentrations in type II hyperlipoproteinemia, but neomycin/niacin, **cholestyramine** and **lovastatin** had the most favorable impact. Only **lovastatin** treatment was free of adverse effects.

CT Check Tags: Comparative Study; Female; Human; Male  
Adult  
Aged  
    **Cholestyramine: AE, adverse effects**  
    **Cholestyramine: TU, therapeutic use**  
    **Drug Therapy, Combination**  
    Hypercholesterolemia: BL, blood  
    \*Hypercholesterolemia: DT, drug therapy  
    Hypercholesterolemia, Familial: DT, drug therapy  
    **Lovastatin**  
    Middle Age  
    Naphthalenes: AE, adverse effects  
    Naphthalenes: TU, therapeutic use  
    Neomycin: AE, adverse effects  
    Neomycin: TU, therapeutic use  
    Niacin: AE, adverse effects  
    Niacin: TU, therapeutic use

## Retrospective Studies

RN 11041-12-6 (**Cholestyramine**); 1404-04-2 (Neomycin); 59-67-6  
(Niacin); 75330-75-5 (**Lovastatin**)  
CN 0 (Naphthalenes)

L173 ANSWER 58 OF 63 MEDLINE

AN 87061360 MEDLINE

DN 87061360 PubMed ID: 3537351

TI Treatment of primary moderate **hypercholesterolemia** with  
**lovastatin** (**mevinolin**) and colestipol.

AU Vega G L; Grundy S M

NC HL-29252 (NHLBI)

M01-RR00633 (NCRR)

SO JAMA, (1987 Jan 2) 257 (1) 33-8.

Journal code: KFR; 7501160. ISSN: 0098-7484.

CY United States

DT (CLINICAL TRIAL)

Journal; Article; (JOURNAL ARTICLE)

LA English

FS Abridged Index Medicus Journals; Priority Journals

EM 198701

ED Entered STN: 19900302

Last Updated on STN: 19970203

Entered Medline: 19870121

AB The introduction of inhibitors of **cholesterol** biosynthesis offers a new approach to treatment of **hypercholesterolemia**. One such agent, **lovastatin** (formerly, **mevinolin**), causes significant reductions in plasma **cholesterol** levels. This action can be enhanced by bile acid sequestrants. In this study, **lovastatin** and colestipol hydrochloride together were administered to ten patients with primary moderate **hypercholesterolemia**. Compared with a control period, the combined-drug therapy caused a 36% reduction in plasma total **cholesterol** level, a 48% decrease in low-density lipoprotein (LDL) **cholesterol** level, and a 17% increase in high-density lipoprotein **cholesterol** level. The reduction in LDL **cholesterol** level was due to three factors: a 27% decrease in the production rate of LDL, a 20% increase in fractional catabolic rate of LDL, and a 15% depletion of **cholesterol** in LDL particles. This major reduction in LDL **cholesterol** level produced by combined-drug therapy may be valuable for prevention of coronary heart disease in high-risk patients with primary moderate **hypercholesterolemia**.

CT Check Tags: Female; Human; Male; Support, Non-U.S. Gov't; Support, U.S. Gov't, Non-P.H.S.; Support, U.S. Gov't, P.H.S.

Aged

\*Anticholesteremic Agents: AD, administration & dosage

Apolipoproteins: BL, blood

Clinical Trials

\*Colestipol: AD, administration & dosage

Drug Therapy, Combination

Hypercholesterolemia: BL, blood

\*Hypercholesterolemia: DT, drug therapy

Kinetics

Lipids: BL, blood

Lipoproteins, HDL Cholesterol: BL, blood

Lipoproteins, LDL Cholesterol: BL, blood

Lovastatin

Middle Age

\*Naphthalenes: AD, administration & dosage

\*Polyamines: AD, administration & dosage

RN 50925-79-6 (Colestipol); 75330-75-5 (**Lovastatin**)

CN 0 (**Anticholesteremic Agents**); 0 (Apolipoproteins); 0 (Lipids); 0  
(Lipoproteins, HDL **Cholesterol**); 0 (Lipoproteins, LDL  
**Cholesterol**); 0 (Naphthalenes); 0 (Polyamines); 0 (apolipoprotein  
LDL)

L173 ANSWER 59 OF 63 MEDLINE

AN 87041897 MEDLINE

DN 87041897 PubMed ID: 3640503

TI Efficacy of **mevinolin** as adjuvant therapy for refractory familial **hypercholesterolaemia**.

AU Thompson G R; Ford J; Jenkinson M; Trayner I

SO QUARTERLY JOURNAL OF MEDICINE, (1986 Aug) 60 (232) 803-11.

Journal code: QKZ; 0401027. ISSN: 0033-5622.

CY ENGLAND: United Kingdom

DT Journal; Article; (JOURNAL ARTICLE)

LA English

FS Priority Journals

EM 198612

ED Entered STN: 19900302

Last Updated on STN: 19900302

Entered Medline: 19861215

AB **Mevinolin**, a potent inhibitor of **cholesterol**synthesis, was used as a therapeutic adjuvant in patients with refractory familial **hypercholesterolaemia** for an average period of 13months. Sustained decreases in serum **cholesterol** of 23 and 31per cent were achieved by doses of 20 mg and 40 mg/day respectively in 13 heterozygotes already on **cholestyramine** or after partial ileal

bypass. Administration of 80 mg/day to three patients undergoing plasma

exchange reduced peak serum **cholesterol** levels by 11.5 per cent

in two homozygotes and by 17 per cent in a double heterozygote for

familial **hypercholesterolaemia** and type IIIhyperlipoproteinaemia. The decrease in **cholesterol** was largelyconfined to low-density lipoprotein and no significant changes occurred in serum triglyceride or high-density lipoprotein **cholesterol**.**Mevinolin** was well-tolerated except in one patient who developed

myositic symptoms; asymptomatic, transient elevations of serum enzymes

were observed in five others. Short and long Synacthen tests showed no

evidence that the drug impaired adrenocortical response to ACTH. These

results indicate that **mevinolin** provides a safe and highly

effective means of reducing LDL levels in patients with heterozygous

familial **hypercholesterolaemia** refractory to conventional

treatment but is less useful in homozygotes.

CT Check Tags: Female; Human; Male

Adult

Aged

Cholesterol: ME, metabolism

Cholestyramine: TU, therapeutic use

Drug Therapy, Combination

Heterozygote

Homozygote

\*Hypercholesterolemia, Familial: DT, drug therapy

Hypercholesterolemia, Familial: ME, metabolism

Hypercholesterolemia, Familial: TH, therapy

Ileum: SU, surgery

Lovastatin

Middle Age

Naphthalenes: AE, adverse effects

\*Naphthalenes: TU, therapeutic use

RN 11041-12-6 (Cholestyramine); 57-88-5 (Cholesterol);

75330-75-5 (Lovastatin)

CN 0 (Naphthalenes)

L173 ANSWER 60 OF 63 MEDLINE

AN 86269217 MEDLINE

DN 86269217 PubMed ID: 3524586

TI The effects of **mevinolin** and neomycin alone and in combination on plasma lipid and lipoprotein concentrations in type II hyperlipoproteinemia.

AU Hoeg J M; Maher M B; Bailey K R; Brewer H B Jr

SO ATHEROSCLEROSIS, (1986 Jun) 60 (3) 209-14.

Journal code: 95X; 0242543. ISSN: 0021-9150.



CY Netherlands  
DT (CLINICAL TRIAL)  
Journal; Article; (JOURNAL ARTICLE)  
LA English  
FS Priority Journals  
EM 198607  
ED Entered STN: 19900321  
Last Updated on STN: 19900321  
Entered Medline: 19860725

AB The reduction of elevated low density lipoprotein (LDL) **cholesterol** concentrations in patients with Type II hyperlipoproteinemia leads to improved cardiovascular morbidity and mortality. Two agents which may be of value in treating **hypercholesterolemia** are **mevinolin** and neomycin. Since these drugs lower **cholesterol** levels through complementary mechanisms, we evaluated the effects of **mevinolin** and combined **mevinolin**-neomycin treatment on plasma lipoprotein concentrations in 21 type II hyperlipoproteinemic patients. **Mevinolin** reduced total and LDL **cholesterol** concentrations by 24% and 31% respectively (P less than 0.001) and 81% of the patients reduced their LDL **cholesterol** levels to less than 200 mg/dl. Although the addition of neomycin to **mevinolin** treatment further lowered total (5%) and LDL (4%) **cholesterol** concentrations, it also reduced HDL **cholesterol** levels (19%) (P less than 0.05). Therefore **mevinolin** normalizes the plasma lipid concentrations in patients with type II hyperlipoproteinemia and combined **mevinolin** and neomycin treatment offers no advantage over **mevinolin**-only therapy. In addition, these findings emphasize the importance of determining the HDL **cholesterol** level to fully evaluate the effects of hypolipidemic therapy.

CT Check Tags: Human  
Clinical Trials  
Drug Interactions  
    **Drug Therapy, Combination**  
    **Hypercholesterolemia, Familial: BL, blood**  
    **Hypercholesterolemia, Familial: DH, diet therapy**  
    **\*Hypercholesterolemia, Familial: DT, drug therapy**  
Lipids: BL, blood  
Lipoproteins: BL, blood  
    **Lipoproteins, HDL Cholesterol: BL, blood**  
    **Lipoproteins, LDL Cholesterol: BL, blood**  
    **Lovastatin**  
    **\*Naphthalenes: AD, administration & dosage**  
    **\*Neomycin: AD, administration & dosage**

RN 1404-04-2 (Neomycin); 75330-75-5 (**Lovastatin**)  
CN 0 (Lipids); 0 (Lipoproteins); 0 (Lipoproteins, HDL **Cholesterol**);  
0 (Lipoproteins, LDL **Cholesterol**); 0 (Naphthalenes)

L173 ANSWER 61 OF 63 MEDLINE  
AN 85277658 MEDLINE  
DN 85277658 PubMed ID: 3849281  
TI Influence of combined therapy with **mevinolin** and interruption of bile-acid reabsorption on low density lipoproteins in heterozygous familial **hypercholesterolemia**.  
AU Grundy S M; Vega G L; Bilheimer D W  
NC HL-29252 (NHLBI)  
MO1-RR 00633 (NCRR)  
SO ANNALS OF INTERNAL MEDICINE, (1985 Sep) 103 (3) 339-43.  
Journal code: 5A6; 0372351. ISSN: 0003-4819.  
CY United States  
DT Journal; Article; (JOURNAL ARTICLE)  
LA English  
FS Abridged Index Medicus Journals; Priority Journals  
EM 198509  
ED Entered STN: 19900320  
Last Updated on STN: 19970203

Entered Medline: 19850909

AB Patients with heterozygous familial **hypercholesterolemia** have a 50% deficiency of receptors for plasma low density lipoproteins (LDL) that induces a marked increase in plasma LDL levels. Two therapeutic measures that seem to increase the synthesis of LDL receptors are interruption of the enterohepatic circulation of bile acids with either bile-acid sequestrants or the ileal-exclusion operation, and competitive inhibition of 3-hydroxy-3-methylglutaryl coenzyme A reductase with **mevinolin** or compactin. To determine the effectiveness of this combination and the mechanisms of lowering LDL levels, we measured turnover rates of LDL apoprotein (apo-LDL) before and during treatment with **mevinolin** and colestipol in eight patients with heterozygous familial **hypercholesterolemia**. Drug therapy reduced LDL **cholesterol** levels by an average of 52%; this response was due to a 40% increase in fractional catabolic rate of apo-LDL and a 26% decrease in its production rate. A similar response was obtained in two patients who had previously had an ileal-exclusion operation for severe **hypercholesterolemia** and who were treated with **mevinolin**.

CT Check Tags: Female; Human; Male; Support, Non-U.S. Gov't; Support, U.S. Gov't, Non-P.H.S.; Support, U.S. Gov't, P.H.S.

Adult

Apolipoproteins: BL, blood

\*Bile Acids and Salts: ME, metabolism

**Cholesterol: BL, blood**

Colestipol: TU, therapeutic use

Combined Modality Therapy

**Drug Therapy, Combination**

Enterohepatic Circulation

Heterozygote

Hydroxymethylglutaryl CoA Reductases: AI, antagonists & inhibitors

**Hypercholesterolemia, Familial: BL, blood**

**Hypercholesterolemia, Familial: DT, drug therapy**

**\*Hypercholesterolemia, Familial: TH, therapy**

Ileum: SU, surgery

Kinetics

**\*Lipoproteins, LDL: BL, blood**

**Lovastatin**

Middle Age

\*Naphthalenes: TU, therapeutic use

RN 50925-79-6 (Colestipol); 57-88-5 (**Cholesterol**); 75330-75-5 (**Lovastatin**)

CN 0 (Apolipoproteins); 0 (Bile Acids and Salts); 0 (Lipoproteins, LDL); 0 (Naphthalenes); 0 (apolipoprotein LDL); EC 1.1.1.88 (Hydroxymethylglutaryl CoA Reductases)

L173 ANSWER 62 OF 63 MEDLINE

AN 85041661 MEDLINE

DN 85041661 PubMed ID: 6388097

TI **Mevinolin** stimulates receptor-mediated clearance of low density lipoprotein from plasma in familial **hypercholesterolemia** heterozygotes.

AU Bilheimer D W; Grundy S M; Brown M S; Goldstein J L

NC HL-15949 (NHLBI)

HL-20948 (NHLBI)

HL-29252 (NHLBI)

SO TRANSACTIONS OF THE ASSOCIATION OF AMERICAN PHYSICIANS, (1983)

96 1-9. Ref: 14

Journal code: W5P; 7506109. ISSN: 0066-9458.

CY United States

DT Journal; Article; (JOURNAL ARTICLE)

General Review; (REVIEW)

LA English

FS Priority Journals

EM 198412

ED Entered STN: 19900320

Last Updated on STN: 19970203

Entered Medline: 19841218

AB The current results show that one can exploit the normal regulation of receptor synthesis to stimulate the single normal gene in FH heterozygotes to produce an increased number of LDL receptors. This stimulation can be achieved by drugs that inhibit HMG CoA reductase in the liver and by maneuvers that cause bile acid depletion. These two therapeutic approaches are most effective when they are combined. It seems reasonable to speculate that such a profound lowering of plasma **cholesterol** levels will minimize the development of atherosclerosis in FH heterozygotes. In a broader sense, the success of this regulatory manipulation raises the possibility that other genetic diseases may be treated through manipulation of regulatory signals that control the rates of synthesis of gene products.

CT Check Tags: Animal; Human; Support, U.S. Gov't, P.H.S.

**Anticholesteremic Agents: PD, pharmacology**

**\*Anticholesteremic Agents: TU, therapeutic use**

**Cholesterol: BI, biosynthesis**

Colestipol: TU, therapeutic use

Combined Modality Therapy

Dogs

**Drug Therapy, Combination**

Heterozygote

**Hypercholesterolemia, Familial: BL, blood**

**\*Hypercholesterolemia, Familial: DT, drug therapy**

**Hypercholesterolemia, Familial: GE, genetics**

**Hypercholesterolemia, Familial: SU, surgery**

Ileum: SU, surgery

**\*Lipoproteins, LDL: BL, blood**

**Lipoproteins, LDL Cholesterol: BL, blood**

Liver: ME, metabolism

**Lovastatin**

Naphthalenes: PD, pharmacology

**\*Naphthalenes: TU, therapeutic use**

**\*Receptors, LDL: BI, biosynthesis**

RN 50925-79-6 (Colestipol); 57-88-5 (**Cholesterol**); 75330-75-5

(**Lovastatin**)

CN 0 (**Anticholesteremic Agents**); 0 (**Lipoproteins, LDL**); 0 (**Lipoproteins, LDL Cholesterol**); 0 (**Naphthalenes**); 0 (**Receptors, LDL**)

L173 ANSWER 63 OF 63 MEDLINE

AN 85020945 MEDLINE

DN 85020945 PubMed ID: 6567462

TI **Mevinolin** plus colestipol in therapy for severe heterozygous familial **hypercholesterolemia**.

AU Illingworth D R

NC HL29074 (NHLBI)

HL32271 (NHLBI)

RR334 (NCRR)

+

SO ANNALS OF INTERNAL MEDICINE, (1984 Nov) 101 (5) 598-604.

Journal code: 5A6; 0372351. ISSN: 0003-4819.

CY United States

DT Journal; Article; (JOURNAL ARTICLE)

LA English

FS Abridged Index Medicus Journals; Priority Journals

EM 198411

ED Entered STN: 19900320

Last Updated on STN: 19970203

Entered Medline: 19841114

AB Twelve patients with severe heterozygous familial **hypercholesterolemia**, in whom other hypolipidemic drug therapy had failed to reduce serum **cholesterol** levels to less than 300 mg/dL, were sequentially treated with **mevinolin** (a specific inhibitor of 3-hydroxy-3-methylglutaryl coenzyme A reductase, the rate-limiting enzyme in **cholesterol** biosynthesis) and

colestipol. In ten patients receiving 80 mg/d of **mevinolin**, plasma **cholesterol** concentrations decreased 33%, from 487 +/- 27 (SE) mg/dL to 326 +/- 16 mg/dL. Additional therapy with colestipol resulted in a further 18% decrease, to 269 +/- 13 mg/dL. Concentrations of low density lipoprotein (LDL) **cholesterol** decreased in parallel (54% decrease on combined drug therapy). Plasma concentrations of high density lipoprotein **cholesterol** did not change significantly, but the LDL:HDL ratio decreased from 8.2 in patients on diet only to 3.8 in patients treated with **mevinolin** and colestipol. In seven patients treated with 40 mg/d of **mevinolin**, concentrations of LDL **cholesterol** decreased by 33%; combined therapy resulted in a further 20% decrease (46% reduction from the level achieved with diet only). No consistent side effects have been noted in up to 24 months of therapy. Combined therapy with **mevinolin** and colestipol promises to be effective for heterozygous familial **hypercholesterolemia**.

CT Check Tags: Female; Human; Male; Support, U.S. Gov't, P.H.S.

Adult

Aged

**Anticholesteremic Agents: AD, administration & dosage**

**\*Anticholesteremic Agents: TU, therapeutic use**

**Cholesterol: BL, blood**

Colestipol: AD, administration & dosage

**\*Colestipol: TU, therapeutic use**

**Drug Therapy, Combination**

Heterozygote

**Hypercholesterolemia, Familial: BL, blood**

**\*Hypercholesterolemia, Familial: DT, drug therapy**

**Lipoproteins, HDL Cholesterol: BL, blood**

**Lipoproteins, LDL Cholesterol: BL, blood**

**Lovastatin**

Middle Age

Naphthalenes: AD, administration & dosage

**\*Naphthalenes: TU, therapeutic use**

**\*Polyamines: TU, therapeutic use**

RN 50925-79-6 (Colestipol); 57-88-5 (Cholesterol); 75330-75-5 (Lovastatin)

CN 0 (Anticholesteremic Agents); 0 (Lipoproteins, HDL Cholesterol); 0 (Lipoproteins, LDL Cholesterol); 0 (Naphthalenes); 0 (Polyamines)

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L219 ANSWER 1 OF 5 WPIX COPYRIGHT 2001 DERWENT INFORMATION LTD

AN 1996-230977 [24] WPIX

DNC C1996-073056

TI Pure high mol. wt. **sulphated polysaccharide** prepn. -  
by filtering and diafiltering aq. mixt. contg. crude prod, used as  
**cholesterol esterase** inhibitor and  
**hypcholesterolaemic** agent.

DC B04 D13

IN LANGE, L G; REARDAN, D T; SPILBURG, C A

PA (CVTH-N) CV THERAPEUTICS INC

CYC 21

PI AU 9534240 A 19960426 (199624)\* 60p C08B005-14  
EP 712864 A2 19960522 (199625) EN 26p C08B037-00  
R: AT BE CH DE DK ES FR GB GR IE IT LI LU MC NL PT SE  
US 5521303 A 19960528 (199627) 18p C07H001-06  
CA 2160440 A 19960414 (199633) C08B005-14  
EP 712864 A3 19961016 (199648) C08B005-14  
JP 08253502 A 19961001 (199649) 21p C08B037-00  
JP 2655592 B2 19970924 (199743) 21p C08B037-00  
AU 682792 B 19971016 (199801) C08B005-14  
CA 2160440 C 19980825 (199845) C08B005-14

ADT AU 9534240 A AU 1995-34240 19951012; EP 712864 A2 EP 1995-307295 19951013;  
US 5521303 A US 1994-322782 19941013; CA 2160440 A CA 1995-2160440  
19951012; EP 712864 A3 EP 1995-307295 19951013; JP 08253502 A JP  
1995-265885 19951013; JP 2655592 B2 JP 1995-265885 19951013; AU 682792 B  
AU 1995-34240 19951012; CA 2160440 C CA 1995-2160440 19951012

FDT JP 2655592 B2 Previous Publ. JP 08253502; AU 682792 B Previous Publ. AU  
9534240

PRAI US 1995-451563 19950526; US 1994-322782 19941013

REP No-SR.Pub; EP 53473; WO 9012579

IC ICM C07H001-06; C08B005-14; C08B037-00  
ICS A23L001-30; **A61K031-72**; **A61K031-725**; C08B003-00

AB AU 9534240 A UPAB: 19960618  
Prepn. of a non-absorbable, very high mol.wt. **sulphated polysaccharide** (I), having **sulphate** to monomer ratio 1.0-3.0, contg. < 5.0 wt.% **sulphates polysaccharides** of mol.wt. < 75000 and contg. < 0.5 wt.% inorganic **sulphate**, involves: (a) admixing water with a dry crude high mol.wt., **sulphated polysaccharide** (II); (b) filtering the obtd. aq. (II) soln.; and (c) diafiltering the filtrate against water using a membrane of mol.wt. cut-off 500000 or more.  
A new (I), having **sulphate** to monomer ratio 2 and average mol.wt. > 2000000, i.e. (I'), is obtd. as above, where the crude starting material (II) has been prepd. by adding DMF/SO3 complex to a suspension reaction at below 20deg.C, adding aq. base and sepg. (II) from DMF and aq. reactants by washing the mixt. with an organic solvent such as acetone.  
Also claimed are: a method of lowering serum **cholesterol** (Ch) in humans by admin. of (I) (specifically (I')) by ingestion; an inhibitor of human Ch absorption comprising a therapeutic amt. of (I); and an inhibitor of human **cholesterol esterase** (CE) comprising 10-5000 mg (I').  
USE - (I) specifically inhibit or decrease intestinal Ch absorption by inhibiting pancreatic CE-catalysed hydrolysis of naturally occurring and ingested Ch esters and by inhibiting CE-facilitated free Ch uptake.  
(I) may be used as drugs or as dietary supplements (esp. with foods rich in Ch and/or its esters) to reduce Ch absorption.  
Therapeutic dose of (I) is 10-5000 mg, pref. incorporated into a food prodn. or administered in a pharmaceutical dosage form selected from tablets, capsules, liquids and powder.  
ADVANTAGE - (I) are potent ( $K_i < 5 \mu M$ ) and safe CE inhibitors. They are not absorbed, do not activate the plasma enzyme lipoprotein lipase and are non-degradable, non-toxic and inexpensive, being derived from cheap (possibly waste) materials.  
The process eliminates toxic low mol.wt. **polysaccharide** and free **sulphate** by-prods.  
(I) do not cause steatorrhoea.

Dwg.0/4

FS CPI

FA AB; DCN

MC CPI: B04-C02; B14-D02A2; B14-D07A; B14-F06; D03-H01T2

ABEQ US 5521303 A UPAB: 19960710

A process for preparing an essentially non-absorbable very high molecular weight **sulphated polysaccharide** having less than about 5.0 wt. percent of **sulphated polysaccharides** having a molecular weight less than 75,000 Daltons, and containing less than 0.5 weight percent of inorganic **sulphate**, comprising the steps;

(a) admixing water with a dry crude high molecular weight **sulphated polysaccharide** to create a crude aqueous **sulphated polysaccharide** solution;

(b) filtering the crude aqueous **sulphated polysaccharide** solution in a first filtering step to produce a filtrate; and

(c) dia-filtering the filtrate of step (b) against water using a membrane having a molecular weight cut-off of 500,000 or greater in a second filtering step to produce a purified very high molecular weight **sulphated polysaccharide**.

Dwg.0/0

L219 ANSWER 2 OF 5 WPIX COPYRIGHT 2001 DERWENT INFORMATION LTD

AN 1996-087083 [09] WPIX

CR 1990-348258 [46]; 1991-178095 [24]

DNC C1996-028151

TI 3-Sulphated-polysaccharide cholesterol  
esterase inhibitor - in baked food product.

DC B04 D13

IN LANGE, L G; SPILBURG, C A

PA (LANG-I) LANGE L G; (SPIL-I) SPILBURG C A

CYC 1

PI US 5484777 A 19960116 (199609)\* 9p A61K031-72 <--

ADT US 5484777 A CIP of US 1989-340868 19890420, Cont of US 1991-718280  
19910620, Cont of US 1992-928510 19920811, US 1993-167725 19931215

FDT US 5484777 A CIP of US 5017565

PRAI US 1991-718280 19910620; US 1989-340868 19890420; US 1992-928510  
19920811; US 1993-167725 19931215

IC ICM A61K031-72

AB US 5484777 A UPAB: 19991221

An ingestible food product comprises a foodstuff and a therapeutic amount of a non-absorbable synthetic 3-sulphated polysaccharide having an IC50 of 0.02nM or less and a MW of at least 500 kDa, the product being baked.

USE - The **sulphated polysaccharide** inhibits human pancreatic **cholesterol esterase**, thereby decreasing intestinal absorption of **cholesterol** and fatty acid.

Dwg.0/3

FS CPI

FA AB; GI

MC CPI: B04-C02; B14-D07A; B14-F06; D03-H01T2

L219 ANSWER 3 OF 5 WPIX COPYRIGHT 2001 DERWENT INFORMATION LTD

AN 1990-348258 [46] WPIX

CR 1991-178095 [24]; 1996-087083 [09]

DNC C1990-151144

TI Inhibition of intestinal **cholesterol** absorption - by oral admin  
of non-absorbable inhibitor of **cholesterol esterase**,  
esp. high mol.wt. **sulphated polysaccharide**.

DC B04 D16

IN LANGE, L G; SPILBURG, C A

PA (LANG-I) LANGE L G; (SPIL-I) SPILBURG C A; (SCHI-I) SCHIERANO P

CYC 17

PI WO 9012579 A 19901101 (199046)\* 49p

RW: AT BE CH DE DK ES FR GB IT LU NL SE

W: AU CA JP US

AU 9055356 A 19901116 (199107)

US 5017565 A 19910521 (199123) 8p

US 5063210 A 19911105 (199147) 11p

EP 469079 A 19920205 (199206)  
 R: AT BE CH DE ES FR GB IT LI LU NL SE  
 JP 04503813 W 19920709 (199234) 19p A61K045-00 <--  
 AU 633569 B 19930204 (199312) A61K031-715 <--  
 EP 469079 B1 19941207 (199502) EN 29p A61K031-72 <--  
 R: AT BE CH DE DK ES FR GB IT LI LU NL SE  
 DE 69014870 E 19950119 (199508) A61K031-72 <--  
 ES 2064736 T3 19950201 (199511) A61K031-72 <--  
 JP 08019001 B2 19960228 (199613) 19p A61K045-00 <--  
 US 5616570 A 19970401 (199719) # 20p A61K031-72 <--  
 CA 2053258 C 19980210 (199817) A61K031-72 <--  
 US 5792832 A 19980811 (199839) C07K007-06  
 ADT US 5017565 A US 1989-340868 19890420; US 5063210 A US 1989-429398  
 19891031; EP 469079 A EP 1990-907923 19900420; JP 04503813 W JP  
 1990-506819 19900420, WO 1990-US2079 19900420; AU 633569 B AU 1990-55356  
 19900420; EP 469079 B1 EP 1990-907923 19900420, WO 1990-US2079 19900420;  
 DE 69014870 E DE 1990-614870 19900420, EP 1990-907923 19900420, WO  
 1990-US2079 19900420; ES 2064736 T3 EP 1990-907923 19900420; JP 08019001  
 B2 JP 1990-506819 19900420, WO 1990-US2079 19900420; US 5616570 A Cont of  
 WO 1990-US2079 19900420, Cont of US 1991-773875 19911018, US 1994-283723  
 19940801; CA 2053258 C CA 1990-2053258 19900420; US 5792832 A Cont of US  
 1989-429398 19891031, Cont of US 1989-434899 19891113, Cont of US  
 1992-856910 19920512, Div ex US 1994-350801 19941207, US 1995-461881  
 19950605  
 FDT JP 04503813 W Based on WO 9012579; AU 633569 B Previous Publ. AU 9055356,  
 Based on WO 9012579; EP 469079 B1 Based on WO 9012579; DE 69014870 E Based  
 on EP 469079, Based on WO 9012579; ES 2064736 T3 Based on EP 469079; JP  
 08019001 B2 Based on JP 04503813, Based on WO 9012579; US 5792832 A Cont  
 of US 5173408  
 PRAI US 1989-429398 19891031; US 1989-340868 19890420; US 1994-283723  
 19940801; US 1989-434899 19891113; US 1992-856910 19920512; US  
 1994-350801 19941207; US 1995-461881 19950605  
 REP 2.Jnl.Ref; DE 1492011; GB 1053143; GB 953626; US 3148114; US 4520017;  
 01Jnl.Ref; GB 1164569; GB 1433732; US 3175942; US 4436731; US 4623539  
 IC ICM A61K031-715; A61K031-72; A61K045-00;  
 C07K007-06  
 ICS A23L001-30; A23L001-308; A61K031-725; A61K031-73;  
 A61K031-795; A61K039-39; A61K039-395;  
 C07K009-00; C12N009-16  
 ICA C12N009-99  
 AB WO 9012579 A UPAB: 19991221  
 Ingestible food prod. contains an effective amt. of a non-absorbable  
 synthetic **cholesterol esterase** inhibitor (I).  
 Inhibiting the intestinal absorption of **cholesterol** comprises  
 admin. p.o. a non-absorbable inhibitor of **cholesterol**  
**esterase** or an antibody directed against **cholesterol**  
**esterase**.  
 Reducing serum **cholesterol** levels comprises admin. of a  
 synthetic non-absorbable **sulphated polysaccharide** in  
 combination with an absorbed **cholesterol** synthesis blocker,  
 triglyceride lipase inhibitor or fatty acyl **cholesterol** O-acyl  
 transferase (ACAT) inhibitor.  
 USE/ADVANTAGE - (I), esp. **sulphonated**  
**polysaccharides**, decrease intestinal absorption of  
**cholesterol** and fatty acid by inhibiting pancreatic  
**cholesterol esterase**, which is a key enzyme involved in  
 dietary **cholesterol** absorption. (I) are stable and can be  
 incorporated in food prods., including baked prods. for dietary control of  
 serum **cholesterol** levels and atherosclerosis (I) are potent  
 inhibitors; are non-absorbable, so that side-effects are reduced; and are  
 inexpensive. Doses of **cholesterol** synthesis blockers or ACAT  
 inhibitors can be reduced, and side-effects minimized, by use with (I).  
 Dwg.0/10  
 FS CPI  
 FA AB  
 MC CPI: B04-B04C6; B04-B04F; B04-C02; B07-A02; B12-G01B2;

B12-G01B3; B12-H03; B12-J01; D03-H01T

ABEQ US 5017565 A UPAB: 19930928

Method of inhibiting human pancreatic **cholesterol esterase** in the alimentary tract comprises oral admin. of a 3-**sulphated polysaccharide** (I). (I) is pref. 3-**sulphated** alginic acid, pectin, amylopectin, chitin, dextran, cellulose agar or chitosan which are all soluble, potent inhibitors of human pancreatic **cholesterol esterase**.

USE - In inhibiting or decreasing **cholesterol** and fatty acid absorption.

In an example, Na alginate (150 mg) was treated with 5 cc glacial acetic acid for 2 hrs. at room temp., filtered and resuspended in 5 ml N,N-dimethylformamide. To stirred soln. 1.5 g SO<sub>3</sub>-pyridine complex was added over 30 mins. at room temp. and resulting mixt. stirred overnight for 16 hrs. 5 ml dry pyridine was then added and the **sulphated** alginic acid was pptd. with 10 ml acetone-MeOH (9:1) mixt. before dissolving in 50 ml H<sub>2</sub>O and adding IN NaOH to adjust pH to 8. Repptn. with 200 ml acetone-MeOH (9:1) mixt. produced the Na salt of **sulphonated** alginic acid. Cpd. was tested for **cholesterol esterase** inhibition and it had IC<sub>50</sub> of 0.25 microg/ml or 1.0nM.

ABEQ US 5063210 A UPAB: 19930928

Inhibiting pancreatic **cholesterol esterase** comprises contacting it with a 3-**sulphate polysaccharide** of M.W. 10+ kDa (100+ kDa, 500+ kDa). Pref. the 3-**sulphated polysaccharide** is 3-**sulphated** alginic acid, pectin, amylopectin, chitin, dextran, cellulose, agar or chitosan (Fig.2). Prepn. is e.g. by treating chitosan with glacial HOAc, dissoln.e in DMFA and sulphonation with SO<sub>3</sub>/pyridine.

USE - The method reduces the absorption of **cholesterol** and triglycerides from the intestine and their concns. in the blood stream so reducing risk of atherosclerosis, etc. The material can be eaten in a baked biscuit.

ABEQ EP 469079 B UPAB: 19950117

Use of a non-absorbable inhibitor of **cholesterol esterase** in the manufacture of an ingestible pharmaceutical composition for inhibiting the intestinal absorption of **cholesterol** wherein said inhibitor is a 3-**sulphated polysaccharide** or an antibody to **cholesterol esterase**.

Dwg.0/7

ABEQ US 5616570 A UPAB: 19970512

A method for inhibiting the intestinal absorption of **cholesterol** in a mammal by administering orally a non-absorbable inhibitor of **cholesterol esterase** comprising a 3-**sulphated polysaccharide** having a molecular weight greater than 100,000 Da.

Dwg.0/7

L219 ANSWER 4 OF 5 WPIX COPYRIGHT 2001 DERWENT INFORMATION LTD

AN 1990-218740 [29] WPIX

DNN N1990-169759 DNC C1990-094452

TI Determn. of net high density lipoprotein **cholesterol** content of serum - by pptn. of other lipoprotein(s) then assaying **cholesterol** in lipase treated and untreated samples, for assessing risk of vascular disease.

DC B04 D13 S03

IN MAINES, R Q

PA (MAIN-I) MAINES R Q

CYC 14

PI EP 378395 A 19900718 (199029)\*

R: AT BE CH DE ES FR GB LI LU NL SE

CA 2007645 A 19900713 (199039)

EP 378395 A3 19920701 (199333)

US 5453358 A 19950926 (199544) 5p C12Q001-60

EP 378395 B1 19960814 (199637) EN 12p C12Q001-60

R: AT BE CH DE DK ES FR GB LI LU NL SE

DE 69028023 E 19960919 (199643) C12Q001-60

ADT EP 378395 A EP 1990-300287 19900110; EP 378395 A3 EP 1990-300287 19900110;



US 5453358 A Cont of US 1989-297080 19890113, US 1992-941669 19920908; EP 378395 B1 EP 1990-300287 19900110; DE 69028023 E DE 1990-628023 19900110, EP 1990-300287 19900110  
 FDT DE 69028023 E Based on EP 378395  
 PRAI US 1989-297080 19890113; US 1992-941669 19920908  
 REP NoSR.Pub; 6.Jnl.Ref; EP 271963; GB 2097255; JP 51139634; JP 61118323; JP 62263119; US 4186251; US 4215993; US 4414326; WO 8905354  
 IC **A61K031-68**; C12Q001-60; G01N033-92  
 ICM C12Q001-60  
 ICS **A61K031-23; A61K031-68; A61K031-685**  
 ICA G01N033-92  
 AB EP 378395 A UPAB: 19931119

Determin. of the net HDL **cholesterol** content of blood serum comprises (1) treating a sample with a pptg. agent which combines with LDL and VLDL particles in the serum; (2) centrifuging to remove ppte., leaving supernatant contg. HDL and free **cholesterol** (Ch); (3) treating supernatant with enzyme which de-esterifies (Ch), so as to break down HDL particles into (Ch) and fatty acid; (4) treating with (Ch) oxidase to oxidise all (Ch) to H<sub>2</sub>O<sub>2</sub> and cholest-4-en-3-one; (5) treating with peroxidase (POD), 4-amine-antipyrine (4AAP) and chromogen to convert the H<sub>2</sub>O<sub>2</sub> produced to a quinone imine (QI); (6) measuring the absorbance of QI at a suitable wavelength; (7) repeating steps (3-6) on at least one (Ch)-contg. standard; (8) calculating the concn. of HDL and non-pptd. (Ch) from the equation (HDL + free (Ch) concn.) = S.C. x 2As/Ast. (As and Ast = absorbance of sample and standard respectively; S.C = concn. of the standard); (9) repeating steps (4-6) on separate samples of supernatant and standard, (10) calculating the non-pptd. free (Ch) concn. from the eqn. free (Ch) concn. = S.C. x 2As/Ast and (11) calculating net HDL **cholesterol** by subtraction of results from steps (8) and (10).

Also new is an emulsified diet supplement for increasing % HDL **cholesterol** in the blood consisting of a polyunsatd. lipid, phospholipid contg. essential fatty acids; a polysaccharide and an antioxidant.

USE - The measurement of HDL **cholesterol** is used to diagnose (and assess the risk of) vascular disease and atherosclerosis. The new diet supplement reduces the risk of such diseases. @9pp  
 Dwg.No.0/0)  
 0/0

FS CPI EPI  
 FA AB; DCN  
 MC CPI: B01-D02; B03-F; B03-H; B04-B01B; B04-B01C1; B04-B02C2; B04-B02C3; B04-B04D4; **B04-C02D**; B04-C03D; B05-B01P; B07-D08; B10-C03; B11-C07B1; **B12-H03**; B12-K04A; D03-C; D05-A02A; D05-A02C  
 EPI: S03-E14H

ABEQ US 5453358 A UPAB: 19951109  
 Determining the level of risk for a patient to vascular disease comprises (a) determining the net percentage of HDL **cholesterol** of blood serum by (i) precipitating LDL and VLDL fractions from a blood serum sample, (ii) sepg. and isolating the precipitant from a supernatant, (iii) treating the supernatant with **cholesterol esterase** or lipase to de-esterify HDL **cholesterol**, (iv) converting all of the **cholesterol** in the supernatant to H<sub>2</sub>O<sub>2</sub> and cholest-4-en-3-one, (v) converting all H<sub>2</sub>O<sub>2</sub> to quinoneimine in the supernatant, (vi) determining the amt. of quinoneimine in the supernatant, (vii) converting the amt. into a concn. of HDL **cholesterol** and free **cholesterol**, (viii) effecting steps (iv)-(vi) on a 2nd sample of the supernatant from step (ii) and converting the amt. into a concn. of free **cholesterol**, and (ix) determining net HDL **cholesterol** by subtracting the concn. of free **cholesterol** from step (viii) from the concn. of HDL **cholesterol** and free **cholesterol** from step (vii), and (b) determining an increased risk of vascular disease for patients exhibiting concns. of net HDL **cholesterol** that are less than 15% of total serum **cholesterol**.

USE - The method is also used for diagnosing atherosclerosis.  
 Dwg.0/0

ABEQ EP 378395 B UPAB: 19960918

A method of determining the net concentration of **cholesterol** associated with HDL particles in blood serum, comprising the steps of (a) treating a sample of the serum with a precipitating agent which will combine with the LDL and VLDL particles in the serum; (b) centrifuging the treated serum sample until the LDL- and VLDL-containing precipitate is spun down, leaving a supernatant liquid having HDL associated **cholesterol**, and free supernatant **cholesterol**; (c) separating the supernatant liquid from the precipitate; (d) treating a first sample of the supernatant liquid with **cholesterol esterase** or lipase in sufficient quantity to break down all the HDL particles into free **cholesterol** and fatty acids, resulting in a **cholesterol**-containing fluid having no esterified **cholesterol**; (e) treating the **cholesterol**-containing fluid with **cholesterol** oxidase in sufficient quantity to oxidise all the **cholesterol** present, forming hydrogen peroxide and cholest-4-en-3-one; (f) further treating the fluid with peroxidase, 4-aminoantipyrine and a chromogen in sufficient amounts to completely react all the hydrogen peroxide formed in step (e) to produce a quinoneimine; (g) measuring the electromagnetic radiation absorbance of the quinoneimine-containing fluid produced in step (h) at a wavelength at which the quinoneimine exhibits significant absorbance; (i) performing steps (d) through (g) on each of one or more standard **cholesterol**-containing fluids; (j) calculating the combined concentration of **cholesterol** associated with the HDL particles, and free supernatant **cholesterol** according to the formula (**cholesterol** associated with HDL + free supernatant **cholesterol** concentration) = standard concentration x  $2(A_{\text{supernatant}})/A_{\text{standard}}$ , where  $A_{\text{supernatant}}$  represents the absorbance measured for the supernatant and  $A_{\text{standard}}$  represents the absorbance measured for the standard **cholesterol**-containing fluid; (k) performing steps (e) through (g) on a second sample of the supernatant liquid, and one or more standard **cholesterol**-containing fluids, (l) calculating the concentration of free supernatant **cholesterol** from the absorbance values obtained in step (j) according to the formula free supernatant **cholesterol** concentration =  $2(A_{\text{supernatant}})/A_{\text{standard}}$  x standard concentration; and (m) calculating the net concentration of **cholesterol** associated with HDL particles from the results of steps (i) and (k) according to the formula net concentration of **cholesterol** associated with HDL = (**cholesterol** associated with HDL + free supernatant **cholesterol** concentration) - free supernatant **cholesterol** concentration.

Dwg.0/0

L219 ANSWER 5 OF 5 WPIX COPYRIGHT 2001 DERWENT INFORMATION LTD

AN 1989-292337 [40] WPIX

DNC C1989-129545

TI Inhibition of intestinal **cholesterol** and fatty acid absorption - by admin. of heparin, its sub-fraction or heparinase.

DC B04 D16

IN KINNUNEN, P M; LANGE, L G; SPILBURG, C A

PA (LANG-I) LANGE L G; (CVTH-N) CV THERAPEUTICS; (JEWI-N) JEWISH HOSPITAL ST

CYC 13

PI WO 8908456 A 19890921 (198940)\* 35p

RW: AT BE CH DE FR GB IT LU NL SE

W: AU JP

AU 8934348 A 19891005 (199001)

US 5352601 A 19941004 (199439) 14p C12N009-16

US 5429937 A 19950704 (199532) 13p C12N009-16

US 5492822 A 19960220 (199613) 12p C12N009-16

ADT WO 8908456 A WO 1989-US787 19890227; US 5352601 A CIP of US 1988-168424

19880315, Cont of US 1989-312255 19890222, Cont of US 1990-544212

19900626, Cont of US 1991-655289 19910214, US 1992-936103 19920826; US

5429937 A CIP of US 1988-168424 19880315, Cont of US 1989-312255 19890222,

Cont of US 1990-544212 19900626, Cont of US 1991-655289 19910214, Div ex

US 1992-936103 19920826, US 1994-311862 19940926; US 5492822 A CIP of US 1988-168424 19880315, Cont of US 1989-312255 19890222, Cont of US 1990-544212 19900626, Cont of US 1991-655289 19910214, Div ex US 1992-936103 19920826, Div ex US 1994-311862 19940926, US 1995-386433 19950210

FDT US 5429937 A Div ex US 5352601; US 5492822 A Div ex US 5352601, Div ex US 5429937

PRAI US 1989-312255 19890222; US 1988-168424 19880315; US 1990-544212 19900626; US 1991-655289 19910214; US 1992-936103 19920826; US 1994-311862 19940926; US 1995-386433 19950210

IC **A61K031-70; A61K037-48**

ICM C12N009-16

ICS **A61K031-70; A61K037-48; A61K037-54**

AB WO 8908456 A UPAB: 19930923

Inhibiting intestinal cell endogenous heparin mediated absorption of **cholesterol** or fatty acids in mammals comprises orally administering heparin, an active heparin subfraction or heparinase.

USE - Heparin can compete for binding to **cholesterol esterase**, displacing the enzyme from the membrane of the intestinal cell and greatly diminishing the intestinal absorption of **cholesterol** and **cholesterol** derived fatty acids. Also exogenous heparin displaces the pancreatic enzymes, such as triglyceride lipase which hydrolyse triglycerides into free fatty acids, from the membrane of the intestinal cell.

6

FS CPI

FA AB; DCN

MC CPI: B04-B02C2; **B04-C02E1**; **B12-H03**; D05-H10

ABEQ US 5352601 A UPAB: 19941122

Recovery of purified human pancreatic **cholesterol**

**esterase** fraction (Mr 52,000) comprises passing a soln. of the crude esterase (pH about 8.2) over or through 2-(diethylamino)ethyl-cellulose, when other esterases are bonded to the solid phase; and collecting the eluate contg. the required fraction. Opt. further purification is possible by binding impurities on hydroxyapatite and heparin-Sepharose adsorbents.

USE/ADVANTAGE - The enzyme catalyses the cleavage of **cholesterol** esters in the presence of heparin, heparinase or their active fragments, inhibiting the absorption of **cholesterol** or fatty acids in intestinal cells. The oral administration of heparin or heparinase provides prophylaxis and therapy for atherosclerosis.

Dwg.0/0

ABEQ US 5429937 A UPAB: 19950818

Soln. of purified human pancreatic **cholesterol esterase**

of mol.wt. 100000 is prepd. from a dialysed soln. contg. protein impurities and similar **cholesterol esterase** protein of various mol.wt. Process comprises (a) chromatographing the soln. obtd. on heparin agarose; (b) washing the impurities away; and (c) eluting and collecting the band contg. prod. of mol.wt. 100000.

USE - Used for inhibiting intestinal **cholesterol** absorption in mammals, and in the treatment of atherosclerosis.

Dwg.0/6

ABEQ US 5492822 A UPAB: 19960329

A method for recovering a solution of purified human pancreatic **cholesterol esterase** having a molecular weight of about 100,000, daltons comprising the steps:

(a) preparing a solution of dialysed human pancreatic cytosol including at least two molecular weight fractions of human pancreatic **cholesterol esterase**, one of which is the 100,000 daltons molecular weight fraction of human **cholesterol esterase**;

(b) passing the solution of dialysed pancreatic cytosol over a hydroxyapatite column and eluting all molecular weight fractions of **cholesterol esterase** present as a single peak to give a first eluent;

(c) passing the first eluent over a gel filtration column and

collecting the 100,000 molecular weight fraction of **cholesterol esterase** as a single peak to give a second eluent including the 100,000 dalton molecular weight fraction of **cholesterol esterase** and protein impurities;

(d) dialysing the second eluent;

(e) passing the dialysed second eluent over a chromatography column containing a chromatography material selected from the group consisting of heparin agarose and heparin-Sepharose: and

(f) washing the chromatography column of step (e) and collecting a third eluent containing the purified **cholesterol**

**esterase** having a molecular weight of about 100,000 daltons.

Dwg.0/6

=> d all abeq tech tot

L224 ANSWER 1 OF 9 WPIX COPYRIGHT 2001 DERWENT INFORMATION LTD

AN 2001-049789 [06] WPIX

DNC C2001-013643

TI Treatment of **hypercholesterolemia** with an unsubstituted polydiallylamine polymer and a **cholesterol**-lowering agent.

DC A96 B05

IN DHAL, P K; HOLMES-FARLEY, S R; HUVAL, C C; PETERSEN, J S

PA (GELT-N) GELTEX PHARM INC

CYC 85

PI WO 2000069445 A1 20001123 (200106)\* EN 33p A61K031-785 <--

RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL  
OA PT SD SE SL SZ UG ZW

W: AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB  
GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU  
LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR  
TT UA UG UZ VN YU ZA ZW

AU 9939880 A 20001205 (200113)

A61K031-785 <--

ADT WO 2000069445 A1 WO 1999-US10568 19990513; AU 9939880 A AU 1999-39880  
19990513, WO 1999-US10568 19990513

FDT AU 9939880 A Based on WO 200069445

PRAI WO 1999-US10568 19990513

IC ICM **A61K031-785**

ICS **A61K045-06**; A61P009-10

AB WO 200069445 A UPAB: 20010126

NOVELTY - Treatment of **hypercholesterolemia** comprises administration of an unsubstituted polydiallylamine polymer (I) and a **cholesterol**-lowering agent (II).

DETAILED DESCRIPTION - Treatment of **hypercholesterolemia** comprises administration of an unsubstituted polydiallylamine polymer (I) and a **cholesterol**-lowering agent (II).

An INDEPENDENT CLAIM is included for the following:

(1) a composition comprising (I) and (II) and optionally a carrier.

ACTIVITY - **Antihypercholesterolemic**

MECHANISM OF ACTION - Bile sequestrants; **Cholesterol** inhibitor

USE - For treatment of **hypercholesterolemia** and atherosclerosis and for reducing serum **cholesterol**

Dwg.0/0

FS CPI

FA AB; GI; DCN

MC CPI: A04-B; A12-V01; B04-C03B; B04-C03D; B07-D03; B07-D05;

**B14-D02A2**

TECH UPTX: 20010126

TECHNOLOGY FOCUS - PHARMACEUTICALS - (II) is a fibrate, nicotinic acid or its derivatives, acifran, azacosterol, benfluorex, approximatelyB-benzalbutyramide, carnitine, chondroitin **sulfate**, clomestron, dexamethasone, **dextran sulfate** sodium, 5,8,11,14,17-eicosapentaenoic acid, eritadenine, furazabol, meglutol, melinamide, mytatrienediol, ornithine, gamma-oryzanol, pantethine, pentaerythritol tetraacetate, alpha-phenylbutyramide, prazosin, probucol,

B-sitosterol, sultosilic acid, piperazine salt, tiadenol, triparanol and/or xenbucin, preferably a fibrate, especially clofibrate, gemfibrozil, fenofibrate and/or bezafibrate, niacin or probucol.

TECHNOLOGY FOCUS - POLYMERS - (I) comprises monomeric units of formula (a) and/or (b) or their salts.

A = A bond or CH<sub>2</sub>

. The polymer is cross-linked by means of 0.5-50 (preferably 2.5-20) weight% a multifunctional cross-linking agent, preferably epichlorohydrin, bis(diallylammonium)dialkylene ion. The polymer is a homo or copolymer, preferably comprising diallylamine, allylamine and triallylamine monomers, especially diallylamine and allylamine monomers.

L224 ANSWER 2 OF 9 WPIX COPYRIGHT 2001 DERWENT INFORMATION LTD

AN 2000-182534 [16] WPIX

CR 2000-171407 [14]; 2000-182521 [14]; 2000-182522 [14]; 2000-182541 [14]; 2000-182547 [14]; 2000-182548 [14]; 2000-205366 [14]

DNC C2000-057146

TI Antilipemic composition used for lowering **cholesterol** comprises anionic **polysaccharide** material containing non-sulfated glucuronic acid.

DC A96 B04

IN BRIESTENSKY, J; KISS, F; SANTAR, I

PA (ALPE-N) ALPENSTOCK HOLDINGS LTD

CYC 87

PI WO 2000004907 A1 20000203 (200016)\* EN 49p A61K031-715 <--  
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL  
OA PT SD SE SL SZ UG ZW

W: AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB  
GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU  
LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR  
TT UA UG US UZ VN YU ZA ZW

AU 9950620 A 20000214 (200029)

A61K031-715 <--

EP 1098654 A1 20010516 (200128) EN

A61K031-715 <--

R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT  
RO SE SI

ADT WO 2000004907 A1 WO 1999-IE70 19990721; AU 9950620 A AU 1999-50620  
19990721; EP 1098654 A1 EP 1999-935019 19990721, WO 1999-IE70 19990721

FDT AU 9950620 A Based on WO 200004907; EP 1098654 A1 Based on WO 200004907

PRAI IE 1998-599 19980721; IE 1998-594 19980721; IE 1998-595  
19980721; IE 1998-596 19980721; IE 1998-597 19980721; IE  
1998-598 19980721

IC ICM A61K031-715

ICS A61K031-78; A61K031-785

AB WO 200004907 A UPAB: 20010522

NOVELTY - Antilipemic composition comprises a biocompatible anionic **polysaccharide** material containing non **sulfated** glucuronic acid.

ACTIVITY - Antilipemic.

MECHANISM OF ACTION - None given.

USE - For lowering **cholesterol**.

ADVANTAGE - Polyanhydroglucuronic acid salts and intermolecular complexes are biocompatible, have low toxicity, no adverse side effects, and lower doses can be used compared with other antilipemic drugs.

Dwg.0/0

FS CPI

FA AB; DCN

MC CPI: A12-V01; B04-C02; B04-C02A; B04-C02B;  
B04-C02D; B04-C02E3; B04-C03B; B04-N02; B04-N04;  
B14-F06

TECH UPTX: 20000330

TECHNOLOGY FOCUS - POLYMERS - Preferred compounds: The polysaccharide is derived from a starch, cellulose or gum, or is of microbial origin. The polysaccharide material comprises polyanhydroglucuronic acid, its salts, copolymers or biocompatible intermolecular complex of it. The complex comprises a complex of:

(a) an anionic component comprising a polysaccharide chain containing glucuronic acid (preferably at least 5% of the basic structural units are glucuronic acid), preferably polyanhydroglucuronic acid, its salts or copolymers, having polymeric chain containing 8-30 wt.% carboxyl groups, with at least 80% of these groups of uronic type, upto 5% carbonyl groups and upto 0.5% bound nitrogen; with molecular mass of the polymeric chain being  $1 \times 10^3$ - $3 \times 10^5$  (preferably  $5 \times 10^3$ - $1.5 \times 10^5$ ) Daltons; and  
 (b) a non protein cationic component comprising a natural, semi-synthetic or synthetic oligomer or polymer, preferably (i) containing nitrogen that either carries a positive charge or has a positive charge induced by contact with (a), preferably derivatives of acrylamide, methacrylamide or their copolymers, a starch, cellulose or gum, preferably guar gum hydroxypropyltrimonium chloride; (ii) a synthetic or semi-synthetic polyamino acid, preferably polylysine, polyarginine or alpha,beta-poly-(N-(2-hydroxyethyl)-DL-aspartamide); (iii) a synthetic anti-fibrinolytic, preferably a hexadimethrine dibromide (polybren); (iv) a natural or semi synthetic peptide, preferably protamine, gelatin or fibrinopeptide or (v) an aminoglucan derivative, preferably fractionated chitin or its de-acetylated derivative chitosan, of microbial origin or isolated from shells of arthropods e.g. crabs.

TECHNOLOGY FOCUS - PHARMACEUTICALS - Preferred composition: The composition also comprises other active agents e.g. an antilipemic agent such as a phospholipid, and is in the form of a tablet, pellet, capsule, granule or microsphere.

L224 ANSWER 3 OF 9 WPIX COPYRIGHT 2001 DERWENT INFORMATION LTD

AN 1998-313690 [28] WPIX

DNC C1998-096807

TI Phytosterol (ester) based **hypcholesterolaemic** agent - containing potentiating agent, e.g. tocopherol, chitosan or DNA, to accelerate serum **cholesterol** lowering effect.

DC B05

IN FABRY, B; WEITKEMPER, N

PA (HENK) HENKEL KGAA

CYC 33

PI DE 19700796 A1 19980604 (199828)\* 6p A61K031-575 <--

WO 9823275 A1 19980604 (199828) DE A61K031-575 <--

RW: AT BE CH DE DK ES FI FR GB GR IE IT LU MC NL PT SE

W: AU BR CA CN CZ HU JP KR MX NO NZ PL RU SI SK US

WO 9823277 A1 19980604 (199828) DE A61K031-70 <--

RW: AT BE CH DE DK ES FI FR GB GR IE IT LU MC NL PT SE

W: AU BR CA CN CZ HU JP KR MX NO NZ PL RU SI SK US

AU 9853229 A 19980622 (199844) A61K031-575 <--

AU 9855531 A 19980622 (199844) A61K031-70 <--

DE 19700796 C2 19981112 (199849) A61K031-575 <--

NO 9902562 A 19990527 (199936) A61K000-00 <--

NO 9902564 A 19990527 (199936) A61K000-00 <--

EP 941097 A1 19990915 (199942) DE A61K031-575 <--

R: BE DE DK ES FI FR GB IT NL SE

EP 952837 A1 19991103 (199951) DE A61K031-70 <--

R: BE DE DK ES FI FR GB IT NL SE

AU 713665 B 19991209 (200009) A61K031-575 <--

AU 714993 B 20000113 (200014) A61K031-70 <--

NZ 335974 A 20000623 (200038) A61K031-355 <--

NZ 335990 A 20001027 (200062) A61K031-73 <--

JP 2001504505 W 20010403 (200126) 14p A61K031-575 <--

ADT DE 19700796 A1 DE 1997-19700796 19970113; WO 9823275 A1 WO 1997-EP6447

19971119; WO 9823277 A1 WO 1997-EP6450 19971119; AU 9853229 A AU

1998-53229 19971119; AU 9855531 A AU 1998-55531 19971119; DE 19700796 C2

DE 1997-19700796 19970113; NO 9902562 A WO 1997-EP6450 19971119, NO

1999-2562 19990527; NO 9902564 A WO 1997-EP6447 19971119, NO 1999-2564

19990527; EP 941097 A1 EP 1997-950201 19971119, WO 1997-EP6447 19971119;

EP 952837 A1 EP 1997-951916 19971119, WO 1997-EP6450 19971119; AU 713665 B

AU 1998-53229 19971119; AU 714993 B AU 1998-55531 19971119; NZ 335974 A NZ

1997-335974 19971119, WO 1997-EP6447 19971119; NZ 335990 A NZ 1997-335990

19971119, WO 1997-EP6450 19971119; JP 2001504505 W WO 1997-EP6447  
 19971119, JP 1998-524239 19971119

FDT AU 9853229 A Based on WO 9823275; AU 9855531 A Based on WO 9823277; EP  
 941097 A1 Based on WO 9823275; EP 952837 A1 Based on WO 9823277; AU 713665  
 B Previous Publ. AU 9853229, Based on WO 9823275; AU 714993 B Previous  
 Publ. AU 9855531, Based on WO 9823277; NZ 335974 A Based on WO 9823275; NZ  
 335990 A Based on WO 9823277; JP 2001504505 W Based on WO 9823275

PRAI DE 1996-19649286 19961128

IC ICM **A61K000-00; A61K031-355; A61K031-575;**  
**A61K031-70; A61K031-73**

ICS **A61K031-7105; A61K031-722; A61P003-06**

ICI A61K031-575, A61K031:355; A61K031-575, A61K031:355

AB DE 19700796 A UPAB: 19980715

Use of an active agent mixture (I) for the preparation of  
**hypocholesterolaemic** agents, is new.

(I) comprises (A) phytosterols and/or phytosterol esters and (B)  
 potentiating agents selected from tocopherols, chitosans, phytosterol  
**sulphates** and/or (deoxy)ribonucleic acids.

Also claimed is the use of gelatin for encapsulating (A) or (I).

USE - (I) is preferably administered orally in gelatin capsules, but  
 may also be used in rectal or vaginal suppositories or dissolved or  
 dispersed in foodstuffs.

ADVANTAGE - (B) (which themselves have no  
**hypocholesterolaemic** activity) potentiate and accelerate the  
 action of (A) in reducing serum **cholesterol** levels.

Encapsulation of (I) or (A) in gelatin allows oral administration  
 without prior art problems of taste and/or consistency.

Dwg.0/0

FS CPI

FA AB; DCN

MC CPI: B01-D02; B03-H; **B04-C02E3**; B04-E02; B04-N02; B14-F06

L224 ANSWER 4 OF 9 WPIX COPYRIGHT 2001 DERWENT INFORMATION LTD

AN 1996-039954 [04] WPIX

DNC C1996-013405

TI Compsn. contg. oligosaccharide(s) that bind to lipoprotein lipase - to  
 prevent its interaction with receptors that would cause cellular uptake of  
 lipoprotein, esp. to treat or prevent atherosclerosis.

DC B04

IN LARNKJR, A; OSTERGAARD, P B; LARNKJAER, A

PA (LARN-I) LARNKJAER A; (OSTE-I) OSTERGAARD P B

CYC 64

PI WO 9533468 A1 19951214 (199604)\* EN 32p A61K031-725 <--  
 RW: AT BE CH DE DK ES FR GB GR IE IT KE LU MC MW NL OA PT SD SE SZ UG  
 W: AM AU BB BG BR BY CA CN CZ EE FI GE HU IS JP KE KG KP KR KZ LK LR  
 LT LV MD MG MN MW MX NO NZ PL RO RU SD SG SI SK TJ TM TT UA UG US  
 UZ VN

AU 9525609 A 19960104 (199613) A61K031-725 <--

ADT WO 9533468 A1 WO 1995-DK217 19950602; AU 9525609 A AU 1995-25609 19950602

FDT AU 9525609 A Based on WO 9533468

PRAI DK 1994-637 19940606

REP 03Jnl.Ref; EP 116801; EP 165569; WO 9004607

IC ICM **A61K031-725**

ICA C08B037-10

AB WO 9533468 A UPAB: 19960129

Compsn. comprises, apart from carrier or diluent, an  
**oligosaccharide** of formula (I): dUAp2S(1=>4)-[alpha-  
 DGlcNp2R16R2(1=>4)-X(1=>4)]n-alpha-D-GlcNp2R16R2, where dUAp2S =  
 4-deoxy-alpha-L-threo-hex-4-eno-pyranosyl-uronic acid, 2-**sulphate**  
 ; alpha-D-GlcNp = alpha-D-2-deoxy-2-amino-glucopyranose; X=  
 Idoap2R2(alpha-L-ido-pyranosyl-uronic acid) or beta-D-GlcAp  
 (beta-D-glucopyranosyl-uronic acid); R1=H, **sulphate** or acetyl;  
 R2= H or **sulphate**, and n is an integer of 3-16. (I) can bind  
 to lipoprotein lipase (LPL) to inhibit interaction between the  
 alpha2-macroglobulin receptor/low density lipoprotein receptor-related  
 protein (alpha2-MR/LRP) and LPL (or its complex with lipoprotein). Such as

interaction would result in uptake of lipoprotein by mammalian cells.

USE - (I) are used to treat or prevent diseases involving interaction between alpha2-MR/LRP (esp. when expressed on smooth muscle cells or macrophages) and LPL (or its complex with lipoprotein), specifically atherosclerosis. (I) is administered at 1-100 mg/kg, given by injection, orally, nasally or rectally.

ADVANTAGE - (I) lock the anticoagulant activity of heparin.

Dwg.0/3

FS CPI  
FA AB; DCN  
MC CPI: **B04-C02E1; B04-C02X; B14-F07**

L224 ANSWER 5 OF 9 WPIX COPYRIGHT 2001 DERWENT INFORMATION LTD

AN 1994-012195 [02] WPIX

CR 1986-103236 [16]

DNC C1994-005571

TI Blood hypolipidaemic agent with low toxicity - contains hyaluronic acid (salt) for treating menopausal disorders, sickness etc..

DC B04

PA (SEGK) SEIKAGAKU KOGYO CO LTD

CYC 1

PI JP 05320058 A 19931203 (199402)\* 8p A61K031-725 <--

JP 06062425 B2 19940817 (199431) 8p A61K031-725 <--

ADT JP 05320058 A Div ex JP 1984-167775 19840813, JP 1992-322870 19840813; JP 06062425 B2 Div ex JP 1984-167775 19840813, JP 1992-322870 19840813

FDT JP 06062425 B2 Based on JP 05320058

PRAI JP 1984-167775 19840813; JP 1992-322870 19840813

IC ICM **A61K031-725**

ICS **A61K031-685; A61K037-02**

AB JP 05320058 A UPAB: 19940223

Blood hypolipidaemic agents comprise hyaluronic acid or its salts. Also claimed are agents comprising 0.01-5 pts.wt. hyaluronic acid or its salts, 1-40 pts.wt. chondroitin **sulphate**, its alkali metal salts, or alkaline earth metal salts, 0.5-20 pts.wt. lecithin, and 35-98.5 pts.wt. proteins.

Other components such as vitamins, plant extracts (e.g. Panax ginseng), amino acids, and minerals can be added. Values of total **cholesterol**, neutral lipids, and phospholipids were lowered in blood samples in an assay using rabbits given for 60 days a feed contg. 5% a compsn. comprising 10% an aq. soln. of 1% Na hyaluronate (mol.wt. 700,000), 15% Na chondroitin **sulphate** (mol.wt. 10,000), 5% lecithin, and 79% soybean proteins.

USE/ADVANTAGE - The agents have low toxicity. The agents are used for the maintenance of physical stamina, recovery from fatigue, for improvement of unpleasant sensations in the stomach and abdominal region, menopausal disorders, sickness caused by drinking, and physical weakness, and for nourishment and toxicity. Agents contg. hyaluronic acid can also exert constipation improving activity.

Dwg.0/0

FS CPI  
FA AB; DCN  
MC CPI: **B04-B01B; B04-C02; B04-N02; B05-B01P; B14-F06**

L224 ANSWER 6 OF 9 WPIX COPYRIGHT 2001 DERWENT INFORMATION LTD

AN 1990-012962 [02] WPIX

DNC C1990-005697

TI Physiological active polysaccharide-adsorbed lipid microspheres - useful as anti-arteriosclerotic agent.

DC B04

PA (MIZU-I) MIZUSHIMA H

CYC 1

PI JP 01294626 A 19891128 (199002)\* 4p

ADT JP 01294626 A JP 1988-124796 19880520

PRAI JP 1988-124796 19880520

IC **A61K009-10; A61K031-72**

AB JP 01294626 A UPAB: 19930928



A physiological active **polysaccharide** has been adsorbed to lipid microspheres.

LM are prepd. by a known method. For example, soybean oil (10g) and egg yolk lecithin (1.2g, contg. a small amt. of phosphatidyl ethanolamine) are pre-emulsified, and glycerol (2.21g) and distilled water are added to make 10 ml in all. The blend is further emulsified and homogenised and sterilised to prepare LM. The anti-arteriosclerotic **polysaccharides** are heparin (low molecular, high molecular), sodium heparin, chondroitin **polysulphate**, heparan **sulphate**, xylan **sulphate**, **dextran sulphate** and other heparinolides. The **polysaccharides** are adsorbed to LM are locally applied to the arteriosclerotic portion with excellent drug delivery system.

USE/ADVANTAGE - The lipid microspheres (LM) are useful as an anti-arteriosclerotic agent.

0/0

FS CPI

FA AB; DCN

MC CPI: B04-B01B; B04-B01C1; **B04-C02**; B10-E04C; **B12-H03**

L224 ANSWER 7 OF 9 WPIX COPYRIGHT 2001 DERWENT INFORMATION LTD

AN 1986-198786 [31] WPIX

DNC C1986-085551

TI Anti thrombotic and lipolytic compsns. - contg. synergistic mixt. of xylan poly **sulphate** and an organic acid.

DC B03

IN BAYOL, A; BLANC, F; LANSEN, J; MAFFRAND, J P; PEREILLO, J M

PA (SNFI) SANOFI SA; (ISTS) SCLAVO SPA

CYC 12

PI FR 2574663 A 19860620 (198631)\* 20p

EP 189696 A 19860806 (198632) FR

R: AT BE CH DE FR GB IT LI LU NL SE

JP 61155329 A 19860715 (198634)

ADT FR 2574663 A FR 1984-20129 19841217; EP 189696 A EP 1985-402522 19851217;

JP 61155329 A JP 1985-275850 19851207

PRAI FR 1984-20129 19841217

REP 3.Jnl.Ref; EP 125152; US 3658969; US 4167562

IC **A61K031-72**

AB FR 2574663 A UPAB: 19930922

Therapeutic compsns. contg. an association of xylene **polysulphates** (I) and an organic acid (II) are new.

(I) is pref. SP 54 (also called PZ68) or a fraction isolated from this, having formula (A) where R is -SO<sub>3</sub>Na or H. This material has a mass between 1000 and 40000. It is a known material, obtd. by **sulphation** of a mixt. of xylenes extracted from beech wood. The acid (II) is pref. di- or poly-carboxylic, esp. citric, isocitric, tartaric, malic or ascorbic acids. The compsns. may be given orally, parenterally, rectally or locally, the unit dose of (I) being 0.030 g - 0.250 g and that of (II) being 0.050-0.250 g. The daily dose of (I) is 0.030g - 1.00 g.

USE/ADVANTAGE - Antithrombotic and lipolytic agents. The association of (I) with (II) has a synergistic effect.

0/0

FS CPI

FA AB

MC CPI: B03-F; **B04-C02D**; B10-C02; B12-C09; B12-H02; **B12-H03**

L224 ANSWER 8 OF 9 WPIX COPYRIGHT 2001 DERWENT INFORMATION LTD

AN 1979-69822B [38] WPIX

TI Intravenous soln. for treating arteriosclerosis - comprising Ringers solution and at least eleven added ingredients.

DC B05

PA (EVER-I) EVERS H R

CYC 5

PI US 4167562 A 19790911 (197938)\*

DE 2934718 A 19800313 (198012)

GB 2029218 A 19800319 (198012)  
FR 2434620 A 19800430 (198024)  
GB 2029218 B 19830126 (198304)  
IL 58017 A 19830515 (198329)  
PRAI US 1978-937533 19780828  
IC **A61K009-08; A61K031-72; A61K033-14;  
A61K037-40**  
AB US 4167562 A UPAB: 19930901  
An intravenous soln. for the treatment of arteriosclerosis consists of the following per 10 ml. of standard Ringers soln.: (a) B-complex, 1,000-5,000 mg.; (b) hydrochloric acid U.S.P., 10-40 mg.; (c) sodium ascorbate, 500-25,000 mg.; (d) pyridoxine hydrochloride, 500-5,000 mg.; (e) magnesium **sulphate**, 100-2,500 mg.; (f) adrenal cortex, 250-2,500 mcg.; (g) magnesium chloride, 250-5000 mg.; (h) thiamin, 100-2,000 mg.; (i) heparin sodium, 2,500-25,000 U.S.P. units; (j) calcium gluconate, 250-2,500 mg.; and (k) calcium d-saccharate, 1.6-5.0 mg.  
Ringers soln. normally contains, per 10 ml., NaCl, 86 mg.; KCl, 3 mg.; and CaCl<sub>2</sub>, 3.3. mg.  
FS CPI  
FA AB  
MC CPI: B03-L; B04-B04G; **B04-C02**; B05-A01B; B05-C07; B07-D04;  
B10-A07; B10-A22; B10-B02D; B10-D03; B12-E01; B12-F01;  
**B12-H03**; B12-M07

L224 ANSWER 9 OF 9 WPIX COPYRIGHT 2001 DERWENT INFORMATION LTD  
AN 1973-64575U [43] WPIX  
TI Oligosaccharide sulphuric acid ester - for treatment of arteriosclerosis.  
DC B04  
PA (CHUG) CHUGAI PHARMACEUTICAL CO  
CYC 4  
PI JP 48048618 A (197343)\*  
DE 2319774 A 19741031 (197445)  
GB 1381426 A 19750122 (197504)  
FR 2226162 A 19741220 (197507)  
PRAI JP 1971-82854 19711021  
IC **A61K027-00; A61K031-72**; C08B027-00  
AB JP 48048618 A UPAB: 19930831  
Title ester is effectively absorbed by the gastrointestinal tract when administered orally in combination with a non-ionic surface active agent. In an example 100 mg **oligosaccharide sulphate** (ave. glucose unit 8, S content 5%) in which glucose is linked in 6-membered and 10 mg polyoxyethylene lauryl alcohol ether were dissolved in 5 ml water, and the soln. was orally administered to a rat. The rate of urinary excretion of the **oligosaccharide sulphate** was 3.0% whereas that in controls receiving only **oligosaccharide sulphate** alone was 0.3%.  
FS CPI  
FA AB  
MC CPI: **B04-C02**; B04-C03; **B12-H03**

=> d all abeq tech tot

L232 ANSWER 1 OF 8 WPIX COPYRIGHT 2001 DERWENT INFORMATION LTD  
AN 1999-527033 [44] WPIX  
DNC C1999-154779  
TI Preparation of 4-(6-(hexylcarbamoyloxy)hexylcarbamoyloxy)-piperidine-1-carboxylic acid 4-phenoxyphenyl ester comprises carbonylation and coupling reaction, then carbonylation/hexylamine reaction, dealkylation and phenoxycarbonylation.  
DC B03  
IN JIRKOVSKY, I  
PA (AMHP) AMERICAN HOME PROD CORP  
CYC 1  
PI US 5952506 A 19990914 (199944)\* 7p C07D211-46  
ADT US 5952506 A Provisional US 1997-44805 19970424, US 1998-62515 19980417

PRAI US 1997-44805 19970424; US 1998-62515 19980417

IC ICM C07D211-46

AB US 5952506 A UPAB: 19991026

NOVELTY - Preparation of 4-(6-(hexylcarbamoxyloxy)hexylcarbamoxyloxy)-piperidine-1-carboxylic acid 4-phenoxyphenyl ester comprises reacting 1-benzyl- (or 1-methyl-) 4-hydroxypiperidine with carbonylating agent and 6-aminohexanol, followed by reaction with a carbonylating agent and hexylamine, followed by dealkylation and concomitant phenoxycarbonylation.

DETAILED DESCRIPTION - Preparation of 4-(6-(hexylcarbamoxyloxy)hexylcarbamoxyloxy)-piperidine-1-carboxylic acid 4-phenoxyphenyl ester (I) comprises:

(a) reacting 1-benzyl-4-hydroxypiperidine or 1-methyl-4-hydroxypiperidine in an aprotic solvent at 0-70 deg. C (optionally in the presence of a tertiary amine) with:

(i) a carbonylating coupling reagent selected from carbonyldiimidazole, disuccinimidyl carbonate, 2,2'-carbonyl-bis(3,5-dioxo-1,2,4-oxazolidine) or 3,3'-carbonyl bis(5-phenyl-1,3-1,3,4-oxadiazole-2(3H)thione) and;

(ii) 6-aminohexanol;

(b) reacting the resultant 4-((6-hydroxyhexyl)carbamoxyloxy)piperidine derivative in an aprotic solvent at 0-70 deg. C (optionally in the presence of a tertiary amine) with:

(i) a carbonylating coupling reagent as above; and

(ii) hexylamine; and

(c) dealkylation and concomitant N-(4-phenoxy)phenoxycarbonylation of the intermediate 4-(6-(hexylcarbamoxyloxy)hexylcarbamoxyloxy)piperidine derivative with 4-phenoxyphenyl chloroformate in an aprotic solvent at 15-110 deg. C to give (I).

ACTIVITY - Antilipemic; antiarteriosclerotic.

MECHANISM OF ACTION - **Sterol-Esterase-Inhibitor;**

**Sterol-O-Acyltransferase-Inhibitor;**

**ACAT-Inhibitor.**

USE - For the large-scale preparation of (I) (claimed). (I) is useful for reducing **cholesterol** absorption and in the treatment of **hypercholesterolemia**, hyperlipidemia and atherosclerosis.

ADVANTAGE - (I) inhibits **cholesterol ester hydrolase** and acylcoenzyme A **cholesterol**

**acyltransferase**. The preparation is carried out without isolation of intermediates and without changing solvents. The preparation gives improved purity, higher yields, lower costs, technical convenience and is less labor and time intensive than the prior art route in EP0635501-A1.

Dwg.0/0

FS CPI

FA AB; GI; DCN

MC CPI: B07-D05; B11-C01; **B14-D02A2**; B14-D06; B14-D07A; B14-F06; B14-F07

TECH UPTX: 19991026

TECHNOLOGY FOCUS - ORGANIC CHEMISTRY - Preferred Preparation: The carbonylating coupling reagent is carbonyldiimidazole, the reactions are carried out in the presence of triethylamine and the aprotic solvent is toluene.

The intermediate from step (a) is either 1-benzyl-4-((6-hydroxyhexyl)carbamoxyloxy)piperidine or 1-methyl-4-((6-hydroxyhexyl)carbamoxyloxy)piperidine. The intermediate from step (b) is either 1-benzyl-4-((6-hexylcarbamoxyloxy)hexylcarbamoxyloxy)piperidine or 1-methyl-4-((6-hexylcarbamoxyloxy)hexylcarbamoxyloxy)piperidine. Step (c) is claimed per se.

L232 ANSWER 2 OF 8 WPIX COPYRIGHT 2001 DERWENT INFORMATION LTD

AN 1999-243579 [20] WPIX

DNN N1999-181297 DNC C1999-070962

TI Reducing mammalian serum total **cholesterol** for treating hyperlipidemia, **hypercholesterolemia** and atherosclerosis.

DC B04 D13 D16 P14

IN CHERUKURI, R S V; CHERUVANKY, R; LYNCH, I E; MCPEAK, P

PA (RICE-N) RICEX CO INC; (RICE-N) RICEX CO

CYC 82

PI WO 9911144 A1 19990311 (199920)\* EN 40p A23K001-00  
 RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL  
 OA PT SD SE SZ UG ZW

W: AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GE  
 GH GM HR HU ID IL IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG  
 MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG  
 US UZ VN YU ZW

AU 9892098 A 19990322 (199931) A23K001-00

US 6126943 A 20001003 (200050) A61K035-78

ADT WO 9911144 A1 WO 1998-US17881 19980828; AU 9892098 A AU 1998-92098  
 19980828; US 6126943 A Provisional US 1997-57870 19970902, US 1998-143159  
 19980828

FDT AU 9892098 A Based on WO 9911144

PRAI US 1997-57870 19970902; US 1998-143159 19980828

IC ICM A23K001-00; A61K035-78

ICS A01K029-00; A01N065-00; C12P001-00

AB WO 9911144 A UPAB: 19990525

NOVELTY - Reducing mammalian serum total **cholesterol**, low density lipoprotein (LDL) **cholesterol**, apolipoprotein B and triglyceride levels, comprises ingesting a stabilized rice bran derivative obtained by enzyme treatment of rice bran, and/or an insolubilized fraction.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for:

(1) preparing enzyme treated stabilized rice bran derivative comprising:

(a) mixing stabilized rice bran with an aqueous solution to form a 15-35% solid rice bran slurry;

(b) adding an enzyme to the slurry to convert starch to dextrin; and

(c) drying the slurry to obtain the stabilized rice bran derivative;

(2) the product of the preparation of (1); and

(3) a method for increasing the high density lipoprotein (HDL)/LDL **cholesterol** ratio in mammalian serum, comprising ingesting a stabilized rice bran derivative obtained by enzyme treatment of rice bran, and/or an insolubilized fraction.

ACTIVITY - Antiarteriosclerotic; Antilipemic.

MECHANISM OF ACTION - The major bioactive components present in the rice bran derivatives are tocopherols, tocotrienols, gamma -oryzanol, phytosterols, polyphenols, inositol, B vitamins, protein, fiber, and fat. The components act mostly synergistically, e.g. by enzyme inhibitions: three enzymes, namely 3-hydroxy-3-methylglutaryl-coenzyme A (HMGCoA) reductase, Acyl coenzyme A transferase (**ACAT**) and esterase are inhibited. HMGCoA reductase, a key enzyme involved in the **cholesterol** biosynthesis is inhibited by the tocotrienols, post transcriptionally, reducing the synthesis of **cholesterol** resulting in low circulating **cholesterol**. Acyl coenzyme A transferase (**ACAT**), inhibition is brought about by:

(a) the prevention of cellular **cholesterol** esterification thereby enriching high density lipoprotein **cholesterol** (HDL) with free **cholesterol**;

(b) elevation of HDL, a positive effect, and decreased synthesis of very low density lipoprotein **cholesterol** (VLDL); and

(c) increased clearance of **cholesterol** as bile acids and bile salts.

The net result is lower circulating **cholesterol**.

**Cholesterol esterases** are inhibited by cycloartenol, a component of -y-oryzanol, resulting in a slower hydrolysis of **cholesterol** esters and decreased absorption. This results in lower circulating total **cholesterol**. gamma -Oryzanol inhibits platelet aggregation, and aortic streaks thus reducing atherosclerosis. Rice bran derivatives contain a significant variety and concentration of antioxidants. Antioxidants such as tocopherols, tocotrienols, gamma -oryzanol, polyphenols as ferulic acid, and lipoic acid are involved in the repair of free radical damage, preventing low density lipoprotein **cholesterol** (LDL) oxidation, resulting in the reduction of vascular damage that can lead to cardiovascular disease. Cycloartenol, a

component of gamma -oryzanol, has a structure similar to **cholesterol** and competes with receptor sites of **cholesterol**. This causes a sequestration of **cholesterol** as bile salts and bile pigments, thus maintaining lower levels of circulating **cholesterol**. Phytosterols and fiber facilitate **cholesterol** sequestration from the body through increased excretion of bile salts and bile acids, resulting in lower levels of circulating **cholesterol**. The protein, fat (with high levels of polyunsaturated and monounsaturated fatty acids), and B vitamins also contribute to the **hypcholesterolemic** effect.

USE - The method is used to treat subjects in which elevated levels of serum total **cholesterol**, LDL-**cholesterol**, VLDL-**cholesterol**, apolipoprotein B and triglyceride levels may lead to hyperlipidemia, cardiovascular disease, atherosclerosis, arteriosclerosis or xanthomatosis.

Dwg.0/0

FS CPI GMPI

FA AB; DCN

MC CPI: B04-A10G; **B14-D02A2**; B14-F01; B14-F06; B14-F07; D03-H01T1; D03-H01T2; D03-L; D05-A01A4; D05-A01B

TECH UPTX: 19990517

TECHNOLOGY FOCUS - PHARMACEUTICALS - Preferred materials: The rice bran derivative comprises 40-60 %w/w dietary fiber. The derivative is an insolubilized fraction comprising (w/w): 1-10% total non-fiber carbohydrate content; 10-20% total fat content; and 15-25% total protein.

TECHNOLOGY FOCUS - FOOD - Preferred materials: The rice bran derivative comprises 40-60 %w/w dietary fiber. The derivative is an insolubilized fraction comprising (w/w): 1-10% total non-fiber carbohydrate content; 10-20% total fat content; and 15-25% total protein.

Preferred method: The aqueous slurry is heated to 100-200 (especially 150-200)degreesF using a steam injection cooker or a heat exchanger, after the enzyme (especially dextranase, a maltase or an alpha-amylase) has been added. The drying is carried out using belt drying, spray drying, drum drying or air drying.

L232 ANSWER 3 OF 8 WPIX COPYRIGHT 2001 DERWENT INFORMATION LTD

AN 1998-609956 [51] WPIX

DNC C1998-182788

TI 4-Carbamoyloxy-piperidine-1-carboxylate ester derivative preparation - in 3 stages from 4-hydroxy-piperidine derivative via new intermediates, used as **cholesterol** absorption inhibitor.

DC B03 B05

IN JIRKOVSKY, I

PA (AMHP) AMERICAN HOME PROD CORP

CYC 79

PI WO 9847870 A1 19981029 (199851)\* EN 14p C07D211-46

RW: AT BE CH DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA  
PT SD SE SZ UG ZW

W: AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GE  
GH HU IL IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW  
MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG UZ VN YU  
ZW

AU 9869469 A 19981113 (199913) C07D211-46

ZA 9803399 A 19991229 (200006) 16p C07D000-00

ADT WO 9847870 A1 WO 1998-US6513 19980331; AU 9869469 A AU 1998-69469 19980331; ZA 9803399 A ZA 1998-3399 19980422

FDT AU 9869469 A Based on WO 9847870

PRAI US 1997-845565 19970424

IC ICM C07D000-00; C07D211-46

ICS C07C068-02; C07C069-96

AB WO 9847870 A UPAB: 19981223

Preparation of 4-[(6-hexylcarbamoyloxy)-hexylcarbamoyl]piperidine-1-carboxylic acid 4-phenoxyphenyl ester (I) comprises: (a) reacting 1-(benzyl or methyl)-4-hydroxypiperidine (II) with a carbonylating coupling reagent and 6-aminohexanol (III) in an aprotic solvent at 0-70

deg. C, optionally in the presence of a tertiary amine; (b) reacting the resultant 1-(benzyl or methyl)-4-[(6-hydroxyhexyl)carbamoyloxy]-piperidine (IV) with hexylamine (V) under the conditions of step (1); and (c) dealkylation and concomitant N-(4-phenoxy)-phenoxy-carbonylation of the intermediate 1-(benzyl or methyl)-4-[6-(hexylcarbamoyloxy)-hexylcarbamoyloxy]piperidine (VI) with 4-phenoxyphenyl chloroformate (VII) in an aprotic solvent 15-110 deg. C. Also claimed are novel intermediates (IV), (VI) and (VII). Step (c) is also claimed as a separate process.

USE - (I), described in EP 635501, inhibits both **cholesterol ester hydrolase** and acyl-coenzyme A **cholesterol acyltransferase**, resulting in a reduction of **cholesterol** absorption. Possible uses include treatment of **hypercholesterolaemia**, hyperlipidaemia and atherosclerosis.

ADVANTAGE - This method utilises a single solvent throughout, requires no purification of intermediates and is suitable for large-scale production. The yield and purity of (I) are higher than in the normal laboratory-scale synthesis and the method is much less labour intensive.

Dwg.0/0

FS CPI  
FA AB; DCN  
MC CPI: B07-D05; B14-F06; B14-F07

L232 ANSWER 4 OF 8 WPIX COPYRIGHT 2001 DERWENT INFORMATION LTD

AN 1995-053622 [08] WPIX

DNC C1995-024413

TI New tris carbamic acid ester(s) are **ACAT** inhibitors - useful for treating e.g. atherosclerosis, familial **hypercholesterolaemia** and hyperlipaemia.

DC B03

IN COMMONS, T J; LACLAIR, C M; STRIKE, D P; COMMONS, T J W

PA (AMHP) AMERICAN HOME PROD CORP

CYC 29

PI EP 635501 A1 19950125 (199508)\* EN 35p C07D295-215

R: AT BE CH DE DK ES FR GB GR IE IT LI LU NL PT SE

AU 9467520	A	19950202	(199513)		C07D211-46
CA 2128116	A	19950122	(199516)		C07D211-46
FI 9403441	A	19950122	(199516)		C07D211-46
BR 9402852	A	19950404	(199520)		C07D207-16
JP 07089934	A	19950404	(199522)	27p	C07D211-46
NZ 264032	A	19951221	(199606)		C07D211-04
ZA 9405214	A	19960327	(199619)	55p	C07D000-00
HU 70942	T	19951128	(199733)		C07D211-46
BR 1100752	A3	19980505	(199825)		C07D401-12
SG 47596	A1	19980417	(199826)		C07D295-215
IL 110302	A	19980615	(199836)		C07D205-04
AU 692157	B	19980604	(199839)		C07D211-46
HU 216790	B	19990830	(199940)		C07D211-46
US 5952354	A	19990914	(199944)		A61K031-445
RU 2130928	C1	19990527	(200027)		C07D211-16
TW 369527	A	19990911	(200035)#		C07D211-06

ADT EP 635501 A1 EP 1994-305305 19940719; AU 9467520 A AU 1994-67520 19940718; CA 2128116 A CA 1994-2128116 19940715; FI 9403441 A FI 1994-3441 19940720; BR 9402852 A BR 1994-2852 19940718; JP 07089934 A JP 1994-165075 19940718; NZ 264032 A NZ 1994-264032 19940718; ZA 9405214 A ZA 1994-5214 19940715; HU 70942 T HU 1994-2108 19940715; BR 1100752 A3 BR 1997-1100752 19970512; SG 47596 A1 SG 1996-3025 19940719; IL 110302 A IL 1994-110302 19940713; AU 692157 B AU 1994-67520 19940718; HU 216790 B HU 1994-2108 19940715; US 5952354 A US 1993-95140 19930721; RU 2130928 C1 RU 1994-26296 19940715; TW 369527 A TW 1994-100154 19940110

FDT AU 692157 B Previous Publ. AU 9467520; HU 216790 B Previous Publ. HU 70942

PRAI US 1993-95140 19930721; TW 1994-100154 19940110

REP 01Jnl.Ref; EP 428385; EP 431321; US 5112859; WO 9313067

IC ICM A61K031-445; C07D000-00; C07D205-04; C07D207-16; C07D211-04; C07D211-06; C07D211-16; C07D211-46; C07D295-215; C07D401-12

ICS A61K031-395; A61K031-40; A61K031-415; A61K031-425; A61K031-435; A61K031-44; A61K031-47; A61K031-495; A61K031-505; A61K031-535;

A61K031-54; A61K031-55; C07D207-10; C07D207-12; C07D211-36;  
 C07D211-44; C07D211-62; C07D223-06; C07D223-08; C07D225-02;  
 C07D295-092; C07D401-14; C07D403-06; C07D403-12; C07D403-14;  
 C07D405-00; C07D405-12; C07D405-14; C07D409-06; C07D409-12;  
 C07D409-14; C07D409-60; C07D413-00; C07D413-12; C07D413-14;  
 C07D417-00; C07D417-12; C07D417-14; C12N009-99

ICI C07D211:46, C07D221:20, C07D401-12; C07D211:46, C07D221:20, C07D307:91,  
 C07D405-14

AB EP 635501 A UPAB: 19950602  
 Tris carbamic acid esters of 4 - 8 membered azacycloalkanols of formula  
 (I) and their salts are new; p = 0 - 4, Z = -Ar1, -Ar1-Ar2-, -Ar1-O-Ar2,  
 -Ar1-S-Ar2, -Ar1-O-C(O)-Ar2, -Ar1-C(O)-O-Ar2, -Ar1-C(O)-Ar2,  
 -Ar1-(CH2)1-20-Ar2, -Ar1-(CH2)1-20-O-Ar2, -Ar1-O-(CH2)1-20-Ar2,  
 -Ar1-(CR6=CR6)1-3-Ar2, -(CR6=CR6)1-3-Ar2 or -Ar1-NR7-Ar2; R6 = H or 1-8C  
 alkyl; R7 = H, 1-8C alkyl, 1-8C alkylcarbonyl or 1-8C alkoxy carbonyl; Ar1,  
 Ar2 = Ph, naphthyl, furanyl, benzofuranyl, pyrazinyl, thienyl,  
 benzothienyl, imidazolyl, benzoxazolyl, thiazolyl, benzthiazolyl,  
 indenyl, indolyl, quinolinyl, benzotriazolyl, carbazolyl, benzimidazolyl  
 or fluorenyl etc. (all opt. substd.); A = a bridging gp. selected from  
 1-20C hydrocarbonyl opt. unsatd. with 1-6 sites of olefinic and/or  
 acetylenic unsaturation, -(CH2)m-W-(CH2)n- or -(CH2)b-Y-(CH2)c-; m, n = 1  
 - 19; m + n = 2 - 20; W = -O-, -S- or NR14; R14 = H, 1-20C alkyl, 1-20C  
 alkylcarbonyl, 1-20C alkoxy carbonyl or benzyl; b, c = 0 - 20; b + c = 1 -  
 20, Y = phenylene, pyridinylene, naphthylene, pyrrolylene or a gp. of  
 formula (ii) - (v) etc.; R15 = H, 1-8C alkyl, 1-20C alkylcarbonyl, 1-20C  
 alkoxy carbonyl or benzyl; R1, R2 = H, 1-8C alkyl, 1-8C alkoxy, 1-8C  
 alkylcarbonyl, OH, CN, 1-8C alkylcarbonyloxy or -(CH2)0-6-NR18R19; R18 =  
 1-8C alkyl, 1-8C alkoxy carbonyl or 1-8C alkylcarbonyl; R19 = H or 1-8C  
 alkyl; R3 = H, 1-8C alkyl or 7-15C arylalkyl; aryl = Ph opt. substd. by  
 1-6C alkyl; R4, R5 = H, 1-20C alkyl, 2-20C alkenyl, 3-10C cycloalkyl,  
 -(CH2)1-20-(3-10C cycloalkyl), -(CH2)1-20-Ar1 or -(CH2)1-20-NR20R21; R20 =  
 1-20C alkyl, 2-20C alkenyl, 1-20C alkylcarbonyl, 1-20C alkoxy carbonyl or  
 benzyl; R21 = H or 1-20C alkyl;

USE - (I) inhibit absorption of **cholesterol** from the  
 intestinal tract and inhibit enzymes **cholesterol ester  
 hydrolase** (CEH) and **acyl-CoA  
 cholesterol acyltransferase (ACAT)**. (I) are  
 useful for treating atherosclerosis, familial  
**hypercholesterolaemia** and hyperlipidaemia.  
 Dwg.0/0

FS CPI  
 FA AB; GI; DCN  
 MC CPI: B06-H; B07-D03; B07-H01; **B14-D02A2**; B14-D06; B14-D07A;  
 B14-F06; B14-F07

L232 ANSWER 5 OF 8 WPIX COPYRIGHT 2001 DERWENT INFORMATION LTD  
 AN 1992-432990 [52] WPIX  
 DNC C1992-192232  
 TI New 1-piperidine carboxylic acid 4-phenoxyphenyl ester derivs. - are CEH  
 and **ACAT** inhibitors for treating **hypercholesterolaemia**  
 , hyperlipaemia, coronary heart disease and atherosclerosis.

DC B03  
 IN COMMONS, T J; STRIKE, D P  
 PA (AMHP) AMERICAN HOME PROD CORP  
 CYC 39  
 PI US 5169844 A 19921208 (199252)\* 10p A61K031-445  
 WO 9313067 A1 19930708 (199328) EN 28p C07D211-46  
 RW: AT BE CH DE DK ES FR GB GR IE IT LU MC NL OA PT SE  
 W: AU BB BG BR CA CS FI HU JP KP KR LK MG MN MW NO NZ PL RO RU SD  
 AU 9334251 A 19930728 (199347) C07D211-46

ADT US 5169844 A US 1991-812512 19911220; WO 9313067 A1 WO 1992-US11287  
 19921210; AU 9334251 A AU 1993-34251 19921210

FDT AU 9334251 A Based on WO 9313067

PRAI US 1991-812512 19911220

REP 2.Jnl.Ref; EP 428385; US 5112859

IC ICM A61K031-445; C07D211-46

ICS A61K031-435; A61K031-495; A61K031-54; C07D401-12; C07D417-12  
 AB US 5169844 A UPAB: 19931118  
 Phenoxyphenyl 1-piperidinecarboxylate derivs. of formula (I) are new. In (I) R1 = H, 1-20C alkyl, 3-20C alkenyl, 3-8C cycloalkyl, 3-8C cycloalkyl-(1-6C)alkyl, phenyl (opt. substd. by 1-6C alkyl, 1-6C alkoxy, halo, NO2, CN or CF3) or phenyl-(1-20C) alkyl (opt. ring substd. by 1-6C alkyl, 1-6C alkoxy, halo, NO2, CN, CF3 or Ph); R2 = H or 1-6C alkyl; or NR1R2 forms a gp. of formula (a): n = 0-2; X = O, S or CR7R8; R7 = H, OH, 1-6C alkyl, 2-6C alkanoyloxy, 1-6C hydroxyalkyl, COOH, 1-16C alkoxy carbonyl(sic) or phenyl (opt. substd. by 1-6C alkyl, 1-6C haloalkyl, 1-6C perhaloalkyl, halo, NO2 or CN); R8 = H or 1-6C alkyl; or R7+R8 completes a 3-7C polymethylene ring; R9 = H, 1-6C alkyl or 2-12C gem dialkyl; R3-R6 = H, 1-6C alkyl, 1-6C alkoxy, halo, NO2, CN, 1-6C perhaloalkyl, 1-16C alkoxy carbonyl(sic) or COOH.

USE - (I) inhibit **cholesterol** ester hydrolase (CEH) and/or acyl coenzyme A:**cholesterol acyltransferase** (

**ACAT**) and so inhibit the formation of **cholesteryl**

esters. Thus (I) interfere with, and prevent, assimilation of **cholesterol** into the lymphatic system and thus the bloodstream.

(I) can be used to treat high serum **cholesterol** levels and associated diseases (e.g. coronary heart disease, atherosclerosis, familial **hypercholesterolaemia** and hyperlipaemia).

0/0

Dwg. 0/0

FS CPI

FA AB; GI; DCN

MC CPI: B07-D05; B12-F02; B12-G01B2; B12-G01B3; **B12-H03**

ABEQ WO 9313067 A UPAB: 19931116

Phenoxyphenyl 1-piperidinecarboxylate derivs. of formula (I) are new. In (I), R1 = H, 1-20C alkyl, 3-20C alkenyl, 3-8C cycloalkyl, 3-8C cycloalkyl-(1-6C)alkyl, phenyl (opt. substd. by 1-6C alkyl, 1-6C alkoxy, halo, NO2, CN or CF3) or phenyl-(1-20C) alkyl (opt. ring substd. by 1-6C alkyl, 1-6C alkoxy, halo, NO2, CN, CF3 or Ph); R2 = H or 1-6C alkyl; or NR1R2 forms a gp. of formula (a): n = 0-2; X = O, S or CR7R8; R7 = H, OH, 1-6C alkyl, 2-6C alkanoyloxy, 1-6C hydroxyalkyl, COOH, 1-16C alkoxy carbonyl (sic) or phenyl (opt. substd. by 1-6C alkyl, 1-6C haloalkyl, 1-6C perhaloalkyl, halo, NO2 or CN); R8 = H or 1-6C alkyl; or R7+R8 completes a 3-7C polymethylene ring; R9 = H, 1-6C alkyl or 2-12C gem dialkyl; R3-R6 = H, 1-6C alkyl, 1-6C alkoxy, halo, NO2, CN, 1-6C perhaloalkyl, 1-16C alkoxy carbonyl (sic) or COOH.

USE - (I) inhibit **cholesterol** ester hydrolase (CEH) and/or acyl coenzyme A:**cholesterol acyltransferase** (

**ACAT**) and so inhibit the formation of **cholesteryl**

esters. Thus (I) interferes with, and prevent, assimilation of **cholesterol** into the lymphatic system and thus the bloodstream.

(I) can be used to treat high serum **cholesterol** levels and associated diseases (e.g. coronary heart disease, atherosclerosis, familial **hypercholesterolaemia** and hyperlipaemia).

Dwg. 0/0

L232 ANSWER 6 OF 8 WPIX COPYRIGHT 2001 DERWENT INFORMATION LTD

AN 1992-133595 [17] WPIX

DNC C1992-062469

TI New tri cyclic heterocyclic derivs. are **ACAT** inhibitors - used for treating **hypercholesterolaemia**, atherosclerosis, myocardial infarction etc..

DC B02

IN IKEDA, H; MEGURO, K; TAWADA, H

PA (TAKE) TAKEDA CHEM IND LTD

CYC 17

PI EP 481243 A 19920422 (199217)\* EN 34p

R: AT BE CH DE DK ES FR GB GR IT LI LU NL SE

CA 2052287 A 19920328 (199223) C07D221-06

JP 05009179 A 19930119 (199311) 21p C07D221-06

US 5264454 A 19931123 (199348) 19p C07D311-92

US 5418239 A 19950523 (199526) 18p A61K031-44



ADT EP 481243 A EP 1991-116099 19910921; CA 2052287 A CA 1991-2052287  
19910926; JP 05009179 A JP 1991-202003 19910812; US 5264454 A US  
1991-765182 19910925; US 5418239 A Div ex US 1991-765182 19910925, US  
1993-117950 19930908

FDT US 5418239 A Div ex US 5264454

PRAI JP 1990-259657 19900927; JP 1991-202003 19910812

REP EP 354994

IC ICM A61K031-44; C07D221-06; C07D311-92

ICS A61K031-35; A61K031-365; A61K031-435; A61K031-47; C07D221-16;  
C07D311-78; C07D311-94

AB EP 481243 A UPAB: 19931006

Fused heterocycle derivs. of formula (I) and their salts are new. Ring A and ring B= opt. substd. benzene; X= N(O)m= C(R2), N(R3)-CO or O-CO; R2= H, alkyl or alkoxy; m= 0-1; R3= H or alkyl; Y= bond, NH, 1-2C alkylene or vinylene; R1= opt. substd. hydrocarbyl; n= 3-6. Ring A and ring B= benzene opt. substd. by 1-4 of halo, 1-6C alkyl (opt. substd. by halo), 1-6C alkoxy (opt. substd. by halo), 1-6C alkylthio (opt. substd. by halo), 1-3C acyloxy, di(1-6C alkyl); amino or OH (esp. A=benzene substd. by 1-3 of halo, 1-6C alkyl or OH and B= benzene). X= N= CR2, NR3CO or OCO, R2= H or 1-6C alkoxy; R3= 1-6C alkyl; Y= NH or 1-2C alkylene; R1= 1-8C alkyl, 3-7C cycloalkyl, 3-7C cycloalkyl-(1-4C) alkyl, 6-10C aryl or 7-16C aralkyl all opt. substd. by 1-5 of halo, 1-6C alkyl (opt. substd. by halo), 1-6C alkoxy, (opt. substd. by halo), 1-6C alkylthio (opt. substd. by halo), 1-3C acyloxy, di(1-6C alkyl) amino or OH (esp. phenyl substd. by 1-3 of halo, 1-6C alkyl, 1-6C alkoxy, 1-6C acyloxy (sic), di(1-6C alkyl)amino or H (partic. 2,4-difluorophenyl)). n=3.

USE - (I) are **acyl-CoA:cholesterol acyl transferase (ACAT)** inhibitors

**ACAT** inhibitors inhibit the absorption of dietary **cholesterol** from the intestinal tract, suppress the increase in **cholesterol** levels in the blood and suppress the accumulator of intracellular **cholesterol**. (I) are useful for treating **hypercholesterolaemia** and atherosclerosis and diseases associated with them e.g. ischaemic heart disease such as myocardial infarction and cerebrovascular disorders such as cerebral infarction and cerebral apoplexy). (0/0)

0/0

FS CPI

FA AB; GI; DCN

MC CPI: B06-H; B12-F01B; B12-F02; B12-G01B2; **B12-H03**

ABEQ US 5264454 A UPAB: 19940120

Heterocyclic derivs. of formula (I) and their salts are new; in which benzene rings A and B are opt. substd. by 1-4 of halo, opt. halogenated 1-6C alkyl, opt. halogenated 1-6C alkoxy, opt. halogenated 1-6C alkylthio, 1-3C acyloxy, di-(1-6C alkyl)amino and OH; X is -O-CO-; Y is a bond, NH or CHCH; R1 is 1-8C alkyl, 3-7C cycloalkyl, (3-7C cycloalkyl)-(1-4C alkyl), 1-6C aryl or 7-6C aralkyl opt. substd. by 1-5 of halo, opt. halogenated (1-6C alkyl, 1-6C alkoxy or 1-6C alkylthio), 1-3C acyloxy, di-(1-6C alkyl)amino and OH; n is 3, 4, 5, 6.

(I) is specifically N-(2,4-difluorophenyl)- N'(4-(2-methylphenyl)-2-oxo-2,6,7,8-tetrahydrocyclopenta (g)(1)benzo- pyran-3-yl) urea.

USE/ADVANTAGE - (I) are **acyl-CoA:cholesterol acyltransferase** inhibitors useful for prevention and treatment of **hypercholesterolemia**, atherosclerosis, ischaemic heart diseases, including myocardial infarction, and cerebrovascular disorders, including cerebral infarction and cerebral apoplexy.

Dwg. 0/0

ABEQ US 5418239 A UPAB: 19950705

Heterocyclic cpds. of formula (I) and their salts are new: where n is 3-6; benzene rings A and B are opt. substd. by 1-4 of: 1 halogen, or 1-6C alkyl, 1-6C alkoxy or 1-6C alkylthio, each opt. halogenated, or 1-3C acyloxy, di-(1-6C alkyl)amino or OH; X is -N(O)m=C(R2)- (in which m is 0 or 1; R2 is H, alkyl or alkoxy), or is -N(R3)-CO- (in which R3 is H or alkyl); Y is a bond, -NH-, 1 or 2C alkylene or -CH=CH-; R1 is 1-8C alkyl, 3-7C cycloalkyl, 3-7C cycloalkyl(1-4C alkyl), 6-10C aryl or 7-16C aralkyl, each

opt. substd. by 1-5 of the substds. as for A and B.

N-(4-(2-Chlorophenyl)-7,8-dihydro-6H-cyclopenta (g)quinolin-3-yl)-N'-(2,4-difluorophenyl)urea is specifically claimed.

USE - Acyl-CoA:cholesterase acyltransferase (ACAT) inhibitor comprises comprising a cpd. (I) and a carrier are claimed, and can be given to a mammal to treat hypercholesterolaemia, atherosclerosis, heart diseases and cerebrovascular disorders.  
Dwg.0/0

L232 ANSWER 7 OF 8 WPIX COPYRIGHT 2001 DERWENT INFORMATION LTD

AN 1990-348258 [46] WPIX

CR 1991-178095 [24]; 1996-087083 [09]

DNC C1990-151144

TI Inhibition of intestinal **cholesterol** absorption - by oral admin of non-absorbable inhibitor of **cholesterol esterase**, esp. high mol.wt. **sulphated polysaccharide**.

DC B04 D16

IN LANGE, L G; SPILBURG, C A

PA (LANG-I) LANGE L G; (SPIL-I) SPILBURG C A; (SCHI-I) SCHIERANO P

CYC 17

PI WO 9012579 A 19901101 (199046)\* 49p

RW: AT BE CH DE DK ES FR GB IT LU NL SE

W: AU CA JP US

AU 9055356 A 19901116 (199107)

US 5017565 A 19910521 (199123) 8p

US 5063210 A 19911105 (199147) 11p

EP 469079 A 19920205 (199206)

R: AT BE CH DE ES FR GB IT LI LU NL SE

JP 04503813 W 19920709 (199234) 19p

A61K045-00 <--

AU 633569 B 19930204 (199312)

A61K031-715 <--

EP 469079 B1 19941207 (199502) EN 29p

A61K031-72 <--

R: AT BE CH DE DK ES FR GB IT LI LU NL SE

DE 69014870 E 19950119 (199508)

A61K031-72 <--

ES 2064736 T3 19950201 (199511)

A61K031-72 <--

JP 08019001 B2 19960228 (199613) 19p

A61K045-00 <--

US 5616570 A 19970401 (199719)# 20p

A61K031-72 <--

CA 2053258 C 19980210 (199817)

A61K031-72 <--

US 5792832 A 19980811 (199839)

C07K007-06

ADT US 5017565 A US 1989-340868 19890420; US 5063210 A US 1989-429398

19891031; EP 469079 A EP 1990-907923 19900420; JP 04503813 W JP

1990-506819 19900420, WO 1990-US2079 19900420; AU 633569 B AU 1990-55356

19900420; EP 469079 B1 EP 1990-907923 19900420, WO 1990-US2079 19900420;

DE 69014870 E DE 1990-614870 19900420, EP 1990-907923 19900420, WO

1990-US2079 19900420; ES 2064736 T3 EP 1990-907923 19900420; JP 08019001

B2 JP 1990-506819 19900420, WO 1990-US2079 19900420; US 5616570 A Cont of

WO 1990-US2079 19900420, Cont of US 1991-773875 19911018, US 1994-283723

19940801; CA 2053258 C CA 1990-2053258 19900420; US 5792832 A Cont of US

1989-429398 19891031, Cont of US 1989-434899 19891113, Cont of US

1992-856910 19920512, Div ex US 1994-350801 19941207, US 1995-461881

19950605

FDT JP 04503813 W Based on WO 9012579; AU 633569 B Previous Publ. AU 9055356, Based on WO 9012579; EP 469079 B1 Based on WO 9012579; DE 69014870 E Based on EP 469079, Based on WO 9012579; ES 2064736 T3 Based on EP 469079; JP 08019001 B2 Based on JP 04503813, Based on WO 9012579; US 5792832 A Cont of US 5173408

PRAI US 1989-429398 19891031; US 1989-340868 19890420; US 1994-283723

19940801; US 1989-434899 19891113; US 1992-856910 19920512; US

1994-350801 19941207; US 1995-461881 19950605

REP 2.Jnl.Ref; DE 1492011; GB 1053143; GB 953626; US 3148114; US 4520017;

01Jnl.Ref; GB 1164569; GB 1433732; US 3175942; US 4436731; US 4623539

IC ICM A61K031-715; A61K031-72; A61K045-00;

C07K007-06

ICS A23L001-30; A23L001-308; A61K031-725; A61K031-73;

A61K031-795; A61K039-39; A61K039-395;

C07K009-00; C12N009-16

ICA C12N009-99

AB WO 9012579 A UPAB: 19991221

Ingestible food prod. contains an effective amt. of a non-absorbable synthetic **cholesterol esterase** inhibitor (I). Inhibiting the intestinal absorption of **cholesterol** comprises admin. p.o. a non-absorbable inhibitor of **cholesterol esterase** or an antibody directed against **cholesterol esterase**.

Reducing serum **cholesterol** levels comprises admin. of a synthetic non-absorbable **sulphated polysaccharide** in combination with an absorbed **cholesterol** synthesis blocker, triglyceride lipase inhibitor or fatty acyl **cholesterol** O-acyl transferase (**ACAT**) inhibitor.

USE/ADVANTAGE - (I), esp. **sulphonated polysaccharides**, decrease intestinal absorption of **cholesterol** and fatty acid by inhibiting pancreatic **cholesterol esterase**, which is a key enzyme involved in dietary **cholesterol** absorption. (I) are stable and can be incorporated in food prods., including baked prods. for dietary control of serum **cholesterol** levels and atherosclerosis (I) are potent inhibitors; are non-absorbable, so that side-effects are reduced; and are inexpensive. Doses of **cholesterol** synthesis blockers or **ACAT** inhibitors can be reduced, and side-effects minimized, by use with (I).

Dwg.0/10

FS CPI

FA AB

MC CPI: B04-B04C6; B04-B04F; **B04-C02**; B07-A02; B12-G01B2; B12-G01B3; **B12-H03**; B12-J01; D03-H01T

ABEQ US 5017565 A UPAB: 19930928

Method of inhibiting human pancreatic **cholesterol esterase** in the alimentary tract comprises oral admin. of a 3-**sulphated polysaccharide** (I). (I) is pref. 3-**sulphated** alginic acid, pectin, amylopectin, chitin, dextran, cellulose agar or chitosan which are all soluble, potent inhibitors of human pancreatic **cholesterol esterase**.

USE - In inhibiting or decreasing **cholesterol** and fatty acid absorption.

In an example, Na alginate (150 mg) was treated with 5 cc glacial acetic acid for 2 hrs. at room temp., filtered and resuspended in 5 ml N,N-dimethylformamide. To stirred soln. 1.5 g SO<sub>3</sub>-pyridine complex was added over 30 mins. at room temp. and resulting mixt. stirred overnight for 16 hrs. 5 ml dry pyridine was then added and the **sulphated** alginic acid was pptd. with 10 ml acetone-MeOH (9:1) mixt. before dissolving in 50 ml H<sub>2</sub>O and adding IN NaOH to adjust pH to 8. Repptn. with 200 ml acetone-MeOH (9:1) mixt. produced the Na salt of **sulphonated** alginic acid. Cpd. was tested for **cholesterol esterase** inhibition and it had IC<sub>50</sub> of 0.25 microg/ml or 1.0nM.

ABEQ US 5063210 A UPAB: 19930928

Inhibiting pancreatic **cholesterol esterase** comprises contacting it with a 3-**sulphate polysaccharide** of M.W. 10+ kDa (100+ kDa, 500+ kDa). Pref. the 3-**sulphated polysaccharide** is 3-**sulphated** alginic acid, pectin, amylopectin, chitin, dextran, cellulose, agar or chitosan (Fig.2). Prepn. is e.g. by treating chitosan with glacial HOAc, dissoln.e in DMFA and sulphation with SO<sub>3</sub>/pyridine.

USE - The method reduces the absorption of **cholesterol** and triglycerides from the intestine and their concns. in the blood stream so reducing risk of atherosclerosis, etc. The material can be eaten in a baked biscuit.

ABEQ EP 469079 B UPAB: 19950117

Use of a non-absorbable inhibitor of **cholesterol esterase** in the manufacture of an ingestible pharmaceutical composition for inhibiting the intestinal absorption of **cholesterol** wherein said inhibitor is a 3-**sulphated polysaccharide** or an antibody to **cholesterol esterase**.

Dwg.0/7

ABEQ US 5616570 A UPAB: 19970512

A method for inhibiting the intestinal absorption of **cholesterol** in a mammal by administering orally a non-absorbable inhibitor of **cholesterol esterase** comprising a **3-sulphated polysaccharide** having a molecular weight greater than 100,000 Da.  
Dwg.0/7

L232 ANSWER 8 OF 8 WPIX COPYRIGHT 2001 DERWENT INFORMATION LTD

AN 1987-039026 [06] WPIX

DNN N1987-029654 DNC C1987-016333

TI Assay of lecithin-**cholesterol acyl-transferase** activity - involves transforming lysolecithin in sample into betaine and hydrogen peroxide and treatment with peroxidase.

DC B04 D16 S03

PA (FUJI-N) FUJIMOTO DIAGNOSTICS

CYC 1

PI JP 61293396 A 19861224 (198706)\* 5p

ADT JP 61293396 A JP 1985-135737 19850620

PRAI JP 1985-135737 19850620

IC C12Q001-44; G01N033-92

AB JP 61293396 A UPAB: 19930922

1st Process: Endogenous lysolecithin in sample is transformed to betaine and H2O2 by reaction of lysolecithin-lipase (LYP), glycerophosphoryl choline phospho-diesterase (GPCP) and cholineoxidase (CHO); and produced H2O2, together with N,N-diethyl-m-toluidine and methyl-p-hydroxybenzoate are treated with peroxidase (POD), and decoloured. 2nd Process:

Lysolecithin produced by lecithin **cholesterolacyl-transferase** (LCAT) from lecithin and free **cholesterol** as substrate, is transformed to betaine and H2O2 by the same enzyme reaction with 1st process, and by peroxide (POD) reaction, produced H2O2, N,N-diethyl-m-toluidine and 4-amino-antipyrine are oxidatively condensated, and quinoid colour is produced. Absorbence of characteristic absorption for the obtd. colour is estimated. In 2nd process, exogenous lecithin is added as substrate, and ester type **cholesterol**, produced with lysolecithin by LCAT reaction is transformed to free **cholesterol** by **cholesterol esterase**.

0/0

FS CPI EPI

FA AB; DCN

MC CPI: B04-B02C2; B04-B02C3; B04-B02C4; B07-D08; B10-B04A; B11-C07B2; B12-K04; D05-A02A; D05-A02B; D05-A02C; D05-H09

EPI: S03-E14H

=> d his

(FILE 'HOME' ENTERED AT 10:59:46 ON 23 JUN 2001)  
SET COST OFF

FILE 'REGISTRY' ENTERED AT 10:59:57 ON 23 JUN 2001

	E CHOLESTEROL/CN
L1	1 S E3
	E CHOLESTEROL ESTERASE/CN
L2	1 S E3
	E LOVASTATIN/CN
L3	1 S E3
L4	1 S E5
	E C24H36O5/MF
L5	12 S E3 AND C6-C6/ES AND OC5/ES AND 3/NR AND BUTANOIC AND 3 7 DIME
L6	11 S L5 NOT 14C
	E C24H38O6/MF
L7	5 S E3 AND C6-C6/ES AND 2/NR AND NAPHTHALENEHEPTANOIC AND 2 6 DIM
L8	4 S L7 NOT 224324-83-8
L9	3 S L8 NOT 101761-41-5
	E CHOLESTEROL ACYLTRANSFERASE/CN

L10 1 S E3

FILE 'HCAPLUS' ENTERED AT 11:10:34 ON 23 JUN 2001

L11 73295 S L1  
L12 1552 S L2  
L13 1355 S CHOLESTEROL ESTERASE  
L14 10 S STEROL ESTERASE  
L15 81 S CHOLESTERASE  
L16 337 S CHOLESTEROL ESTER HYDROLASE  
L17 234 S CHOLESTERYL ESTER HYDROLASE  
L18 94 S CHOLESTERYL ESTERASE  
L19 25 S CHOLESTEROLESTERASE OR CHOLESTERYLESTERASE  
L20 113 S LYSOSOMAL ACID LIPASE  
L21 2194 S L12-L20  
L22 1384 S L3 OR L6 OR L4 OR L9  
L23 1988 S LOVASTATIN OR MEVINOLIN OR MONACOLIN# K OR LOVASTATIN ACID  
L24 43 S MEVACOR OR MEVINOLINIC ACID  
L25 2058 S L22-L24  
L26 1482 S L10  
L27 3574 S CHOLESTEROLACYLTRANSFERASE OR (CHOLESTEROL OR CHOLESTERYL) ( )  
L28 3 S STEROL O ( ) (ACYLTRANSFERASE OR ACYL TRANSFERASE)  
L29 1322 S ACYL COA CHOLESTEROL (1W) (ACYLTRANSFERASE OR ACYL TRANSFERASE)  
L30 5 S ACYL COA ( ) (CHOLESTEROLACYLTRANSFERASE OR CHOLESTERYLACYLTRA  
L31 1078 S ACAT  
L32 3968 S L26-L31  
L33 8 S L21 AND L25  
L34 272 S L21 AND L32  
L35 8 S (L11 OR CHOLESTEROL) AND L33  
L36 2 S L35 AND ?SACCHARID?  
L37 1 S L36 NOT 3/SC  
E HEIDER/AU  
L38 1 S HEIDER ?/AU AND 1983/PY AND (24 AND 1127)/SO

FILE 'REGISTRY' ENTERED AT 11:34:37 ON 23 JUN 2001

L39 1 S 71806-22-9  
E C31H48N2O3/MF  
L40 8 S E3 AND NC4-C6/ES  
L41 5 S L40 AND TRYPTOPHAN AND ETHYL ESTER  
L42 5 S L39, L41  
SEL RN  
L43 0 S E1-E5/CRN

FILE 'HCAPLUS' ENTERED AT 11:37:15 ON 23 JUN 2001

SET SMARTSELECT ON  
L44 SEL L37 1- RN : 13 TERMS  
SET SMARTSELECT OFF

FILE 'REGISTRY' ENTERED AT 11:37:15 ON 23 JUN 2001

L45 13 S L44  
L46 8 S L45 AND S/ELS

FILE 'HCAPLUS' ENTERED AT 11:37:34 ON 23 JUN 2001

L47 8 S L42  
L48 1 S L47 AND L1, L21  
L49 3 S L47 AND L25, L32  
L50 6 S L47 AND ?CHOLEST?  
L51 6 S L48-L50  
L52 2 S L47 NOT L51  
L53 2795 S L46  
SCA L\*\*\*  
L54 5395 S (CHITIN OR CELLULOSE OR DEXTRAN OR CHITOSAN OR AMYLOPECTIN OR  
E POLYSACCHARIDE/CT  
E E14+ALL  
L55 943 S E3, E4 (L) (SULFAT? OR SULPHAT?)  
L56 329560 S E3+NT  
L57 33516 S L56 AND (?SULFAT? OR ?SULPHAT?)

L58 6917 S L56 AND (?SULFONAT? OR ?SULPHONAT?)  
L59 332085 S L53-L58  
L60 162 S L59 AND L25,L32  
L61 10 S L60 AND L21  
L62 6 S L61 AND (1 OR 63)/SC,SX  
L63 3 S L62 NOT (3 OR 6)/SC,SX  
L64 2 S L63 NOT HEPATOCYTES/TI  
L65 0 S L47 AND L59  
E LANGE L/AU  
L66 102 S E3,E6,E18-E20  
E SPILBURG C/AU  
L67 37 S E4-E7  
E REARDAN D/AU  
L68 10 S E4-E6  
L69 19 S L66-L68 AND L11  
L70 24 S L66-L68 AND L21  
L71 1 S L66-L68 AND L25  
L72 6 S L66-L68 AND L32  
L73 14 S L66-L68 AND L59  
L74 38 S L69-L73  
L75 29 S L74 AND (PY<=1994 OR PRY<=1994 OR AY<=1994)  
L76 5 S L75 AND (1 OR 63)/SC,SX  
L77 6 S L37,L38,L64,L76  
L78 8 S L47-L52  
L79 5 S L78 AND (PY<=1994 OR PRY<=1994 OR AY<=1994)  
L80 1 S L79 AND L21,L59  
L81 8 S L78,L79,L80  
SEL HIT RN

L82 FILE 'REGISTRY' ENTERED AT 11:58:17 ON 23 JUN 2001  
7 S E1-E7

L83 FILE 'HCAPLUS' ENTERED AT 11:59:05 ON 23 JUN 2001  
13 S L37,L77,L81  
SEL HIT RN

L84 FILE 'REGISTRY' ENTERED AT 12:00:27 ON 23 JUN 2001  
27 S E8-E34  
L85 40 S L3,L6,L4,L9,L84

FILE 'REGISTRY' ENTERED AT 12:01:32 ON 23 JUN 2001

FILE 'HCAPLUS' ENTERED AT 12:03:07 ON 23 JUN 2001

FILE 'EMBASE' ENTERED AT 12:03:54 ON 23 JUN 2001.

L86 44670 S L1  
L87 87655 S (CHOLESTEROL BLOOD LEVEL OR CHOLESTEROL METABOLISM+NT OR CHOL  
L88 109835 S L86,L87  
L89 701 S L2  
L90 1049 S L21  
L91 1049 S L89,L90  
L92 231 S POLYSACCHARIDE SULFATE/CT  
L93 64665 S POLYSACCHARIDE+NT/CT  
L94 1902 S L46  
L95 2944 S L54  
L96 153 S ESTERASE INHIBITOR/CT  
L97 48421 S ESTERASE INHIBITOR+NT/CT  
L98 4191 S L3,L6,L4,L9  
L99 4404 S L23 OR L24  
L100 6 S L154803 OR L154819 OR L() (154803 OR 154819 OR 154() (803 OR 81  
L101 0 S MK819 OR MK 189  
E MEVACOR  
L102 371 S E1-E4,E6  
L103 984 S L10  
L104 2926 S L27-L31  
L105 333 S CHOLESTEROL ACYLTRANSFERASE INHIBITOR+NT/CT

L106 0 S L42  
L107 187 S L98-L105 AND L91  
L108 5058 S L98-L105 AND L88  
L109 0 S L107,L108 AND L92  
L110 62 S L107,L108 AND L93  
L111 9 S L107,L108 AND L94  
L112 20 S L107,L108 AND L95  
L113 73 S L107,L108 AND L110-L112  
L114 37 S L113 AND PY<=1994  
L115 9 S L114 AND (DRUG COMBINATION OR DRUG POTENTIATION)/CT  
L116 21 S L114 AND (COADMIN? OR COMEDI? OR COPRESCRI? OR COTHERAP? OR C  
L117 9 S L115 AND CB/CT  
L118 21 S L115-L117  
L119 7 S L118 AND ?SULFAT?  
L120 1 S L118 AND ?SULPHAT?  
L121 0 S L118 AND ?SULPHONAT?  
L122 0 S L118 AND ?SULFONAT?  
L123 8 S L119,L120  
L124 416 S (MEVINOLIN(L)CB)/CT  
L125 684 S MEVINOLIN/CT AND (DRUG POTENTIATION OR DRUG COMBINATION)/CT  
L126 684 S L124,L125  
L127 0 S L126 AND L92  
L128 1 S L126 AND L94  
L129 1 S L126 AND L95  
L130 12 S L126 AND L93  
L131 12 S L128-L130  
L132 3 S L105 AND L92-L95  
L133 8 S L105 AND L96,L97  
L134 11 S L132,L133  
L135 13 S L131,L134 AND PY<=1994  
L136 10 S L88 AND L135  
L137 10 S L136 AND (COADMIN? OR COMEDI? OR COPRESCRI? OR COTHERAP? OR C  
L138 4 S L137 NOT AB/FA  
L139 12 S L46,L54 AND L104 AND PY<=1994  
L140 507 S L46,L54 AND (?SACCHARIDE?(S) (?SULFATE? OR ?SULPHAT? OR ?SULFO  
L141 375 S L140 AND PY<=1994  
L142 10 S L88 AND L141  
L143 9 S L139 AND L88  
L144 18 S L142,L143  
L145 17 S L144 NOT DEXTRAN (5A) COLUMN  
L146 11 S L145 AND ?CHOLESTER?  
L147 6 S L145 NOT L146  
L148 11 S L86-L145 AND L146

FILE 'EMBASE' ENTERED AT 12:34:08 ON 23 JUN 2001

FILE 'MEDLINE' ENTERED AT 12:34:36 ON 23 JUN 2001

L149 84 S ((CHOLESTEROL ESTERASE ) (L) AI)/CT  
L150 239067 S D9.203.698./CT  
L151 1356 S L2 OR L21  
L152 71166 S L1 OR CHOLESTEROL/CT  
L153 44605 S (HYPERCHOLESTEROLEMIA+NT OR LIPOPROTEINS, HDL+NT OR LIPOPROTE  
L154 1 S L42  
L155 2924 S L25  
E MEVACOR  
L156 33 S E3-E7  
E LOVASTATIN  
L157 2840 S E1-E12  
L158 3 S E13,E14  
E MEVINOLIN  
L159 310 S E3-E8  
E MONACOLIN  
L160 22 S E3,E4  
L161 1629 S L155-L160 AND L149-L153  
L162 995 S L161 AND PY<=1994  
L163 89 S L162 AND (DRUG COMBINATIONS+NT OR DRUG THERAPY, COMBINATION+N

L164 83 S L163 AND LOVASTATIN+NT/CT  
L165 9 S L164 NOT AB/FA  
SEL DN 5-9  
L166 5 S E1-E10  
L167 74 S L164 NOT L165  
L168 74 S L167 AND ANTICHOLESTEREMIC AGENTS+NT/CT  
L169 63 S L168 AND HYPERLIPIDEMIA+NT/CT  
L170 55 S L168 AND HYPERCHOLESTEROLEMIA+NT/CT  
L171 63 S L169,L170  
L172 11 S L168 NOT L171  
L173 63 S L171 AND ?CHOLEST?  
L174 6606 S ?SACCHARID? (L) (?SULFATE? OR ?SULFONATE? OR ?SULPHATE? OR ?S  
L175 1201 S L46  
L176 2665 S L54  
L177 6433 S L174-L176 AND PY<=1994  
L178 4682 S L177 AND L149-L153  
L179 1 S L178 AND L149  
L180 4 S L178 AND L151  
L181 277 S L178 AND L153  
L182 233 S L178 AND L153/MAJ  
L183 21697 S (POLYSACCHARIDES+NT(L) TU) /CT  
L184 0 S L183/MAJ AND L182  
L185 1 S L183 AND L182

FILE 'MEDLINE' ENTERED AT 13:12:16 ON 23 JUN 2001

FILE 'WPIX' ENTERED AT 13:16:05 ON 23 JUN 2001

L186 13404 S ?CHOLESTER?  
L187 14771 S P814/M0,M1,M2,M3,M4,M5,M6  
L188 9292 S (B12-H03 OR C12-H03 OR B14-D02A2 OR C14-D02A2)/MC  
L189 23514 S L186-L188  
L190 245 S L23,L24  
E LOVASTATIN  
L191 180 S E1-E6  
E MEVINOLIN  
L192 66 S E1-E6  
E MONACOLIN  
L193 24 S E3,E4  
E LOVASTATIN/DCN  
E E3+ALL  
L194 164 S E2  
E MEVACOR  
L195 2 S E3  
L196 235 S L189 AND L190-L195  
L197 216 S L13-L20  
L198 1 S L197 AND L196  
L199 397 S L27-L31  
L200 804 S L54  
L201 2601 S L174  
E CHITIN/DCN  
E E3+ALL  
L202 428 S E2  
L203 315 S E4  
L204 1 S E6  
L205 947 S E8  
L206 315 S E10  
E AMYLOPECTIN/DCN  
E PECTIN/DCN  
E E3+ALL  
L207 523 S E2  
E AGAR/DCN  
E E4+ALL  
L208 421 S E2  
E ALGIN/DCN  
E E4+ALL  
L209 1833 S E2 OR 1866/DRN



L210 403 S E4  
L211 5 S E6  
E DEXTRAN/DCN  
E E5+ALL  
L212 193 S E2  
L213 46 S E4  
L214 11 S E6  
L215 31939 S (V71? OR V72? OR V73?)/M0,M1,M2,M3,M3,M4,M5,M6  
L216 31846 S (B04-C02? OR C04-C02?)/MC  
L217 1574 S L200-L216 AND L189  
L218 21 S L217 AND L197  
L219 5 S L218 AND A61K/IC

FILE 'WPIX' ENTERED AT 13:31:15 ON 23 JUN 2001

L220 1044 S L217 AND A61K/IC NOT L218  
L221 695 S L220 AND M782/M0,M1,M2,M3,M4,M5,M6  
E A61K031-7/IC  
L222 205 S A61K031-7?/IC AND L221  
L223 37 S L222 AND (?SULFAT? OR ?SULPHAT? OR ?SULFONAT? OR ?SULPHONAT?)  
L224 9 S L223 NOT (FIBROBLAST OR PLASTER OR CARDIOVASCULAR OR ANTACID  
L225 183 S L196 AND A61K/IC  
L226 183 S L225 NOT L219,L223  
L227 92 S L226 AND M782/M0,M1,M2,M3,M4,M5,M6  
L228 0 S L227 AND ?ESTERASE?  
L229 216 S L13-L20  
L230 8 S L199 AND L229  
L231 8 S L230 AND L189  
L232 8 S L231 AND L186-L230